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Title of Invention:

Inventors (please provide full names):

Earliest Priority Filing Date:

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Jan,

Please search claims 1-3

Thanks

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=> d l35 all tot

L35 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:658369 HCAPLUS
DN 137:197854
TI **Diagnostics**, assay methods and amelioration of **muscular dystrophy** symptoms
IN **Kaufman, Stephen J.**
PA The Board of Trustees of the University of Illinois, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-68
ICS C12Q001-68; C12N005-00; C12N015-00; A61P021-00; A61K048-00
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 1, 3, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002066989	A2	20020829	WO 2002-US6376	20020220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2002192710	A1	20021219	US 2002-81855	20020221
PRAI	US 2001-270645P	P	20010221		
	US 2001-286491P	P	20010426		

AB The present disclosure provides compns. and sequences for the **diagnosis**, genetic therapy of certain **muscular dystrophies**, esp. **muscular dystrophy** resulting from a deficiency in **dystrophin** protein or a combined deficiency in **dystrophin** and utrophin, and methods and compns. for the identification of compds. which increase expression of the **.alpha**

.7 **integrin**. Expression of the **integrin** .alpha.7X2 polypeptide in muscle cells results in better phys. condition in a patient or an animal lacking normal levels of **dystrophin** or **dystrophin** and utrophin. The present disclosure further provides immunol. and nucleic acid based methods for the **diagnosis** of **scapuloperoneal muscular dystrophy**, where there is a redn. in or absence of .**alpha.7A** **integrin** expression in muscle tissue samples and normal levels of laminin-2/4 in those same samples. The present disclosure further provides methods for identifying compns. which increase the expression of .**alpha.7** **integrin** protein in muscle cells of **dystrophy** patients. Muscle biopsies from 5 patients with **scapuloperoneal muscular dystrophy** were analyzed for **integrin** expression using immunofluorescence and western blot analyses. There was a marked redn. or absence of the .**alpha.7.beta.** **integrin** in all 5 patients as compared with normal healthy controls. In contrast, the .**alpha.7.beta.** **integrin** was detected in the lining of the blood vessels. Using an anti-.**alpha.7A** polyclonal antibody, little or no fluorescence signal was detected in all the samples. The .beta.1D **integrin** expression was normal.

ST **diagnosis** treatment **muscular dystrophy** **alpha7 integrin**; **scapuloperoneal muscular dystrophy diagnosis alpha7 integrin** muscle

IT Laminins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Laminins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(4; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT **Muscular dystrophy**
(**Duchenne**; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT PCR (polymerase chain reaction)
(RT-PCR (reverse transcription-PCR); **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT **Animal tissue**
(anal. of; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Chimeric gene
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(animal, with human .**alpha.7** **integrin** regulatory sequence; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Gene, animal
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric, with human .**alpha.7** **integrin** regulatory sequence; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Animal
DNA sequences
Diagnosis
Disease models
Drug delivery systems
Drug **screening**

Gene therapy
Genetic vectors
Genotyping (method)
Human
Immunoassay
Muscle
Muscular dystrophy
Nucleic acid hybridization
Perfusion
Plasmids
Samples
Southern blot hybridization
Viral vectors
(**diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Primers (nucleic acid)
Reporter gene
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT **Dystrophin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT High throughput **screening**
(drug; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT mRNA
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(for **integrin .alpha.7.beta.1**; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Gene, animal
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(for **integrin .alpha.7.beta.1**; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Proteins
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(green fluorescent, reporter gene coding sequence for; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Drug **screening**
(high throughput; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms

IT Immunoassay
(immunoblotting; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms

IT Immunoassay
(immunofluorometric; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms

IT Drug delivery systems
(infections, i.m.; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms

IT Drug delivery systems
(injections, i.v.; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms

IT CD antigens
Integrins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**integrin .alpha.7, .alpha.7B2**; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT CD antigens
Integrins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**integrin .alpha.7**; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Antibodies
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(labeled, to .alpha.7.beta.1; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Antibodies
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT **Animal tissue culture**
(muscle, with reporter gene; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Gene, animal
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(regulatory, for human **.alpha.7 integrin** gene in reporter construct; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Antigens
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reporter gene coding sequence for tag; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Cell
(reporter gene expression in; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT **Muscular dystrophy**
(scapuloperoneal; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Cell
(stem, **.alpha.7 integrin**-expressing, treatment with; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Antibodies
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to .alpha.7.beta.1; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Mouse
(transgenic; **diagnostics** and assay methods and amelioration of **muscular dystrophy** symptoms)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(utrophins; **diagnostics** and assay methods and amelioration of

muscular dystrophy symptoms
IT Myoblast
.alpha.7 integrin-expressing, treatment with; diagnostics and assay methods and amelioration of muscular dystrophy symptoms
IT Integrins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.alpha.7A; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
IT Integrins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.alpha.7.beta.1; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.1; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
IT 452108-83-7 452108-84-8
RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence RT-PCR primer; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
IT 453615-67-3P
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence, reporter construct contg.; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
IT 9001-45-0P, .beta.-Glucuronidase 9014-00-0P, Luciferase 9031-11-2P, .beta.-Galactosidase 9073-60-3P, .beta.-Lactamase
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reporter gene coding sequence for; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
IT 453661-46-6 453661-47-7 453661-48-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; diagnostics, assay methods and amelioration of muscular dystrophy symptoms)

L35 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:517820 HCAPLUS
DN 137:292866
TI Integrin .alpha.7.beta.1 in muscular dystrophy: myopathy of unknown etiology
AU Pegoraro, Elena; Cepollaro, Fulvio; Prandini, Paola; Marin, Alessandra; Panin, Marina; Trevisan, Carlo P.; El-Messlemani, Abdul Hassib; Tarone, Guido; Engvall, Eva; Hoffman, Eric P.; Angelini, Corrado
CS Neuromuscular Center, University of Padova, Padua, 35128, Italy
SO American Journal of Pathology (2002), 161(1), 215-224
CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB To investigate the role of integrin .alpha.7

in muscle pathol., we used a "candidate gene" approach in a large cohort of **muscular dystrophy**/myopathy patients. Antibodies against the intracellular domain of the **integrin** .alpha .7A and .**alpha**.7B were used to stain muscle biopsies from 210 patients with **muscular dystrophy**/myopathy of unknown etiol. Levels of .**alpha**.7A and .**alpha**.7B **integrin** were found to be decreased in 35 of 210 patients (.apprx.17%). In six of these patients no **integrin** .**alpha**.7B was detected. **Screening** for .**alpha**.7B mutation in 30 of 35 patients detected only one **integrin** .**alpha**.7 missense mutation (the mutation on the second allele was not found) in a patient presenting with a congenital **muscular dystrophy**-like phenotype. No **integrin** .**alpha**.7 gene mutations were identified in all of the other patients showing **integrin** .**alpha**.7 deficiency. In the process of mutation anal., we identified a novel **integrin** .**alpha**.7 isoform presenting 72-bp deletion. This isoform results from a partial deletion of exon 21 due to the use of a cryptic splice site generated by a G to A missense mutation at nucleotide position 2644 in **integrin** .**alpha**.7 cDNA. This spliced isoform is present in about 12% of the chromosomes studied. We conclude that secondary **integrin** .**alpha**.7 deficiency is rather common in **muscular dystrophy**/myopathy of unknown etiol., emphasizing the multiple mechanisms that may modulate **integrin** function and stability.

ST **integrin** isoform mutation **muscular dystrophy** myopathy

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ITGA7; genetics study of **integrin** .**alpha**.7 .**beta**.1 in **muscular dystrophy**/myopathy of unknown etiol.)

IT Mutation
(deletion; genetics study of **integrin** .**alpha**.7.**beta**.1 in **muscular dystrophy**/myopathy of unknown etiol.)

IT **Diagnosis**
(**genetic**; **genetics** study of **integrin** .**alpha**.7.**beta**.1 in **muscular dystrophy**/myopathy of unknown etiol.)

IT Genotypes
Human
Muscular dystrophy
Phenotypes
(genetics study of **integrin** .**alpha**.7 .**beta**.1 in **muscular dystrophy**/myopathy of unknown etiol.)

IT mRNA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**integrin** .**alpha**.7.**beta**. gene; genetics study of **integrin** .**alpha**.7.**beta**.1 in **muscular dystrophy**/myopathy of unknown etiol.)

IT Mutation
(missense; genetics study of **integrin** .**alpha**.7.**beta**.1 in **muscular dystrophy**/myopathy of unknown etiol.)

IT Mutation
(splice site; genetics study of **integrin** .**alpha**.7.**beta**.1 in **muscular**

dystrophy myopathy of unknown etiol.
IT **Integrins**
RL: BSU (Biological study, unclassified ; BIOL (Biological study
.alpha.7A and **.alpha.7B**
isoforms; genetics study of **integrin .alpha.**
7.beta.1 in **muscular**
dystrophy/myopathy of unknown etiol.)
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L38 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:272011 HCAPLUS
DN 128:88809
TI Mutations in the **integrin .alpha.7** gene

cause congenital myopathy

AU Hayashi, Yukiko K.; Chou, Fan-Li; Engvall, Eva; Ogawa, Megumu; Matsuda, Chie; Hirabayashi, Shinichi; Yokochi, Kenji; Ciesker, Barry L.; Kramer, Randall H.; **Kaufman, Stephen J.**; Ozawa, Eijiro; Goto, Yu-Ichi; Nonaka, Ikuya; Tsukahara, Toshifumi; Wang, Jian-Chou; Hoffman, Eric P.; Arahata, Kiichi

CS Department of Neuromuscular Research, National Center of Neurology and Psychiatry, National Institute of Neuroscience, Tokyo, 187-8502, Japan

SO Nature Genetics (1998), 19(1), 94-97
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America
DT Journal
LA English
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 14

AB The basal lamina of muscle fibers plays a crucial role in the development and function of skeletal muscle. An important laminin receptor in muscle is **integrin .alpha.7.beta.1**. **Integrin .beta.1** is expressed throughout the body, while **integrin .alpha.7** is more muscle-specific. To address the role of **integrin .alpha .7** in human muscle disease, the authors detd. **.alpha. 7** protein expression in muscle biopsies from 117 patients with unclassified congenital myopathy and congenital **muscular dystrophy** by immunocytochem. The authors found three unrelated patients with **integrin .alpha.7** deficiency and normal laminin .alpha.2 chain expression. To det. if any of these three patients had mutations of the **integrin .alpha. 7** gene, ITGA7, the authors cloned and sequenced the full-length human ITGA7 cDNA, and **screened** the patients for mutations. One patient had splice mutations on both alleles; one causing a 21-bp insertion in the conserved cysteine-rich region, and the other causing a 98-bp deletion. A second patient was a compd. heterozygote for the same 98-bp deletion, and had a 1-bp frame-shift deletion on the other allele. A third showed marked deficiency of ITGA7 mRNA. Clin., these patients showed congenital myopathy with delayed motor milestones. These results demonstrate that mutations in ITGA7 are involved in a form of congenital myopathy.

ST ITGA7 gene mutation **integrin alpha7** myopathy

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(ITGA7; mutations in **integrin .alpha.7** gene cause congenital myopathy)

IT **Muscle, disease**
(congenital; mutations in **integrin .alpha.7** gene cause congenital myopathy)

IT Mutation
(deletion; mutations in **integrin .alpha.7** gene cause congenital myopathy)

IT Mutation
(insertion; mutations in **integrin .alpha.7** gene cause congenital myopathy)

IT CD antigens
CD antigens
Integrins
Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**integrin .alpha.7**; mutations in **integrin .alpha.7** gene cause congenital myopathy)

IT Mutation
(splice site; mutations in **integrin .alpha.**

7 gene cause congenital myopathy.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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=> d l36 all tot

L36 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:823352 HCAPLUS
DN 134:365225
TI Enhanced expression of the .alpha.7.beta.
1 integrin reduces muscular dystrophy
and restores viability in dystrophic mice
AU Burkin, Dean J.; Wallace, Gregory Q.; Nicol, Kimberly J.; Kaufman, David J.; Kaufman, Stephen J.
CS Department of Cell and Structural Biology, University of Illinois, Urbana, IL, 61801, USA
SO Journal of Cell Biology (2001), 152(6), 1207-1218
CODEN: JCLBA3; ISSN: 0021-9525
PB Rockefeller University Press
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
AB Muscle fibers attach to laminin in the basal lamina using two distinct mechanisms: the dystrophin glycoprotein complex and the .
alpha.7.beta.1 integrin.
Defects in these linkage systems result in Duchenne muscular
dystrophy (DMD , .alpha.2 laminin congenital muscular
dystrophy, sarcoglycan-related muscular
dystrophy, and .alpha.7 integrin
congenital muscular dystrophy. Therefore, the mol.
continuity between the extracellular matrix and cell cytoskeleton is essential for the structural and functional integrity of skeletal muscle.

To test whether the .alpha.7.beta.1 **integrin** can compensate for the absence of **dystrophin**, we expressed the rat .alpha.7 chain in mdx utr-/- mice that lack both **dystrophin** and utrophin. These mice develop a severe **muscular dystrophy** highly akin to that in DMD, and they also die prematurely. Using the muscle creatine kinase promoter, expression of the .alpha.7BX2 **integrin** chain was increased 2.0-2.3-fold in mdx/utr-/- mice. Concomitant with the increase in the .**alpha.7** chain, its heterodimeric partner, .beta.1D, was also increased in the transgenic animals. Transgenic expression of the .alpha.7BX2 chain in the mdx/utr-/- mice extended their longevity by threefold, reduced kyphosis and the development of muscle disease, and maintained mobility and the structure of the neuromuscular junction. Thus, bolstering .**alpha.7.beta.1** **integrin**-mediated assocn. of muscle cells with the extracellular matrix alleviates many of the symptoms of disease obsd. in mdx/utr-/- mice and compensates for the absence of the **dystrophin**- and utrophin-mediated linkage systems. This suggests that enhanced expression of the .**alpha.7.beta.1** **integrin** may provide a novel approach to treat DMD and other muscle diseases that arise due to defects in the **dystrophin** glycoprotein complex.

ST **integrin alpha7beta1** muscle viability Duchenne **muscular dystrophy**

IT **Muscular dystrophy**
(Duchenne; .**alpha.7.beta.1 integrin** increased expression reduces **muscular dystrophy** and restores viability in **dystrophic** mice)

IT CD antigens
Integrins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**integrin .alpha.7**; .**alpha.7.beta.1 integrin** increased expression reduces **muscular dystrophy** and restores viability in **dystrophic** mice)

IT Mouse
(mdx/utr-/-; .**alpha.7.beta.1 integrin** increased expression reduces **muscular dystrophy** and restores viability in **dystrophic** mice)

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(utrophins; .**alpha.7.beta.1 integrin** increased expression reduces **muscular dystrophy** and restores viability in **dystrophic** mice)

IT Cytoskeleton
Disease models
Extracellular matrix
Muscle
Neuromuscular junction
.**alpha.7.beta.1 integrin** increased expression reduces **muscular dystrophy** and restores viability in **dystrophic** mice

IT **Dystrophin**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
.**alpha.7.beta.1 integrin** increased expression reduces **muscular**

dystrophy and restores viability in **dystrophic** mice)
IT **Integrins**
RL: BAC (Biological activity or effector, except adverse ; BIO (Biological occurrence) ; BPR (Biological process ; BSU (Biological study, unclassified) ; BIOL (Biological study ; OCCU (Occurrence) ; PROC (Process
(**.alpha.7.beta.1**;
.alpha.7.beta.1 integrin
increased expression reduces **muscular dystrophy** and restores viability in **dystrophic** mice)
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L36 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:697992 HCAPLUS
DN 135:150306
TI Transfection of MCF-7 carcinoma cells with human **integrin** .**alpha**.7 cDNA promotes adhesion to laminin
AU Vitiriankis, Ioannis S.; Yao, Chung-Chen; Chen, YaoQi; Zieber, Barry L.; Tsiftsoglou, Asterios S.; Kramer, Randall H.
CS Departments of Stomatology and Anatomy, University of California at San Francisco, San Francisco, CA, 94143-0512, USA
SO Archives of Biochemistry and Biophysics (2001), 385(1), 108-116
CODEN: ABBIA4; ISSN: 0003-9861
PB Academic Press
DT Journal
LA English
CC 15-2 (Mammalian Biochemistry
Section cross-reference(s): 3, 6
AB The laminin-binding .**alpha**.7.**beta**.1 **integrin** receptor is highly expressed by skeletal and cardiac muscles, and has been suggested to be a crucial mol. during myogenic cell migration and differentiation. Absence of **integrin** .**alpha**.7 subunit contributes to a form of **muscular dystrophy** in **integrin** .**alpha**.7 null mice, whereas specific mutations in the .**alpha**.7 gene are assocd. in humans with congenital myopathy. To examine in more detail the potential role of **integrin** .**alpha**.7 in human-related muscular disorders, we cloned .**alpha**.7 cDNA by RT-PCR from human skeletal muscle mRNA and then expressed the full-length human **integrin** .**alpha**.7 cDNA by transfection in several cell lines including MCF-7, COS-7, and NIH3T3 cells. The isolated cDNA corresponds to the human .alpha.7X2B alternative splice form. Expression of human .**alpha**.7 was further confirmed by transfection of chimeric human/mouse .**alpha**.7 cDNA constructs. To demonstrate the functionality of expressed human .**alpha**.7, adhesion expts. with transfected MCF-7 cells have confirmed the specific binding of human .**alpha**.7 to laminin. In addn., mouse polyclonal and monoclonal antibodies were generated against the extracellular domain of human .**alpha**.7 and used to analyze by flow cytometry MCF-7 and NIH3T3 cells transfected with the full-length of human .**alpha**.7 cDNA. These results show for the first time the exogenous expression of functional full-length human .**alpha**.7 cDNA, as well as the development of monoclonal antibodies against the human .**alpha**.7 extracellular domain. Antibodies developed will be useful for further anal. of human disorders involving .**alpha**.7 dysfunction and facilitate isolation of muscle stem cells (satellite cells) and thereby expand the opportunities for genetically modified transplantation treatment of human disease. (c) 2001 Academic Press.
CT human **integrin alpha7** cDNA sequence; transfection carcinoma cell human **integrin alpha7** laminin
ST Animal cell line
MCF-7; transfection of MCF-7 carcinoma cells with human **integrin** .**alpha**.7 cDNA promotes adhesion to laminin
IT RNA splicing

(alternative, of **.alpha.7**; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT Neoplasm
(cell, **.alpha.7** expression in; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT cDNA sequences
(for human **integrin .alpha.7** isoform; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT CD antigens
Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**integrin .alpha.7**; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT **Muscle, disease**
(model; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT Antibodies
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(monoclonal, against human **.alpha.7** extracellular domain; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT Protein sequences
(of human **integrin .alpha.7** isoform; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT Cell adhesion
Transformation, genetic
(transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT 204786-84-5, **Integrin .alpha.-7** (human heart)
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

IT 222253-34-1, GenBank AF072132
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L36 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:253680 HCAPLUS
DN 133:57092
TI Laminin .alpha.4 and **Integrin** .alpha.6 Are Upregulated in Regenerating dy/dy Skeletal Muscle: Comparative Expression of Laminin and **Integrin** Isoforms in Muscles Regenerating after Crush Injury
AU Sorokin, Lydia M.; Maley, Moira A. L.; Moch, Helga; von der Mark, Helga; von der Mark, Klaus; Cadalbert, Laurence; Karosi, Stefanie; Davies, Marilyn J.; McGeachie, John K.; Grounds, Miranda D.
CS Interdisciplinary Center for Clinical Research (IZKF), University of Erlangen-Nuremberg, Germany
SO Experimental Cell Research (2000), 256(2), 500-514
CODEN: ECREAL; ISSN: 0014-4827
PB Academic Press
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
AB The expression of laminin isoforms and laminin-binding **integrin** receptors known to occur in muscle was investigated during myogenic regeneration after crush injury. Comparisons were made between **dystrophic** 129ReJ dy/dy mice, which have reduced laminin .alpha.2 expression, and their normal littermates. The overall histol. pattern of regeneration after crush injury was similar in dy/dy and control muscle, but proceeded faster in dy/dy mice. In vitro studies revealed a greater yield of mononuclear cell. extd. from dy/dy muscle and a reduced proportion of desmin-pos. cells upon in vitro cultivation, reflecting the presence of inflammatory cells and "preactivated" myoblasts due to ongoing regenerative processes within the endogenous **dystrophic** lesions. Laminin .alpha.1 was not detectable in skeletal muscle. Laminin .alpha.2 was present in basement membranes of mature myofibers and newly formed

myotubes in control and dy/dy muscles, albeit weaker in dy/dy. Laminin .alpha.4-neg. myogenic cells were detected in dy/dy and control muscle, suggesting the involvement of other laminin .alpha. chains in early myogenic differentiation, such as laminin .alpha.4 and .alpha.5 which were both transiently expressed in basement membranes of newly formed myotubes of dy/dy and control mice. **Integrin .beta.1** was expressed on endothelial cells, muscle fibers, and peripheral nerves in uninjured muscle and broadened after crush injury to the interstitium where it occurred on myogenic and nonmyogenic cells. **Integrin** .alpha.3 was not expressed in uninjured or regenerating muscle, while **integrin** .alpha.6 was expressed mainly on endothelial cells and peripheral nerves in uninjured muscle. Upon crush injury **integrin** .alpha.6 increased in the interstitium mainly on nonmyogenic cells, including infiltrating leukocytes, endothelial cells, and fibroblasts. In dy/dy muscle, **integrin** .alpha.6 occurred on some newly formed myotubes. **Integrin .alpha.7** was expressed on muscle fibers at the myotendinous junction and showed weak and irregular expression on muscle fibers. After crush injury, **integrin .alpha.7** expression extended to the newly formed myotubes and some myoblasts. However, many myoblasts and newly formed myotubes were **integrin .alpha.7** neg. No marked difference was obsd. in **integrin .alpha** .7 expression between dy/dy and control muscle, either uninjured or after crush injury. Only laminin .alpha.4 and **integrin** .alpha.6 expression patterns were notably different between dy/dy and control muscle. Expression of both mols. was more extensive in dy/dy muscle, esp. in the interstitium of regenerating areas and on newly formed myotubes. In view of the faster myogenic regeneration obsd. in dy/dy mice, the data suggest that laminin .alpha.4 and **integrin** .alpha.6 support myogenic regeneration. However, whether these accelerated myogenic effects are a direct consequence of the reduced laminin .alpha.2 expression in dy/dy mice, or an accentuation of the ongoing regenerative events in focal lesions in the muscle, requires further investigation. (c) 2000 Academic Press.

ST laminin alpha4 **integrin** alpha6 **dystrophic** muscle regeneration crush injury

IT Blood vessel
(endothelium; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT **Muscle**
(fiber; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Leukocyte
(inflammatory; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT **Muscle, disease**
(injury; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury

IT CD antigens
CD antigens
Integrins
Integrins

RL: BSC (Biological occurrence ; BSU (Biological study, unclassified ; BIOL (Biological study ; OCCU (Occurrence

integrin .alpha.7; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy

dystrophic skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT **Muscular dystrophy**
Regeneration, animal
(laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury)

IT **Basement membrane**
Cell differentiation
Fibroblast
Myoblast
(laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Desmins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT **Muscle**
Muscle
Tendon
Tendon
(muscle-tendon junction; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT **Muscle**
(myotubule; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Nerve
(peripheral; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Laminins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha.4, .alpha.1, .alpha.2, .alpha.5 chains; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury)

IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.alpha.3; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT **Integrins**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha.6; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury

IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

.beta.1; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating ay dy **dystrophic** skeletal muscle with reduced laminin .alpha.4 expression after crush injury in relation to

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L56 ANSWER 4 OF 10 MEDLINE COPYRIGHT 2003 ACS
AN 1999:84481 MEDLINE
DN 1999220000
TI Organization of the myotendinous junction is dependent on the presence of **.alpha.7.beta.1 integrin**
AU Miosge, Nicolai; Kleinschar, Christina; Herken, Rainer; Willem, Michael; Mayer, Ulrike
CS Zentrum Anatomie, Martinsried, 82152, Germany
SO Laboratory Investigation (1999), 79(12), 1591-1599
CODEN: LAINAW; ISSN: 0023-6837
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 13-1 (Mammalian Biochemistry)
AB The laminin receptor **.alpha.7.beta.1** is enriched at the myotendinous junctions, and mice with a targeted inactivation of the **.alpha.7** gene develop a form of **muscular dystrophy** that primarily affects this structure. By ultrastructural anal. of **.alpha.7** -deficient mice, in comparison with wild-type and mdx mice, we attempted to elucidate the role of **.alpha.7 integrin** for the integrity and function of the myotendinous junctions. Ultrastructurally, myotendinous junctions of **.alpha.7** -deficient myofibers lose their interdigitations and the myofilaments retract from the sarcolemmal membrane, whereas the lateral side of the myofibers remains morphol. normal. The basement membrane at the myotendinous junctions in **.alpha.7** -/- mice is significantly broadened, and immunogold-histochem. has demonstrated that the laminin .alpha.2 chain is not localized here but, instead, in the matrix of the neighboring tendon. In contrast, mdx mice have normal myotendinous junctions, with a matrix protein pattern also found in wild-type mice; however, the lateral sides of the myofibers are severely damaged. These results suggest that the **.alpha.7. beta.1 integrin** is a major receptor connecting the muscle cell to the tendon and helps to organize the myotendinous junction, whereas the **dystrophin**-glycoprotein complex is necessary for the lateral integrity of the muscle cell.
ST myotendinous junction basement membrane laminin nidogen **integrin alpha7 beta1**
IT **Muscle**
(fiber; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha. 7.beta.1 integrin**)
IT CD antigens
CD antigens
Integrins
Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**integrin .alpha.7**; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha.7.beta.1 integrin**)
IT **Muscle**
Muscle
Tendon
Tendon
(muscle-tendon junction; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha.7.beta.1 integrin**)

IT Organelle
  (myofilament; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha. 7.beta.1 integrin**)

IT Entactin
  RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
  (nidogen, 1; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha. 7.beta.1 integrin**)

IT **Basement membrane**
  Tendon
  (organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha.7 .beta.1 integrin**)

IT Cell membrane
  (sarcolemma; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha. 7.beta.1 integrin**)

IT Laminins
  RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
  (.alpha.2 chain; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha. 7.beta.1 integrin**)

IT **Integrins**
  RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
  (**.alpha.7.beta.1**; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of **.alpha.7.beta. 1 integrin**)

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L36 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:637728 HCAPLUS
DN 131:335367
TI Activation of c-Raf-1 kinase signal transduction pathway in **.alpha .7 integrin**-deficient mice
AU Saher, Gesine; Hildt, Eberhard
CS Max-Planck-Institut fur Biochemie, Martinsried, D-82152, Germany
SO Journal of Biological Chemistry (1999), 274(39), 27651-27657
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
AB **Integrin .alpha.7**-deficient mice develop a novel form of **muscular dystrophy**. Here we report that deficiency of **.alpha.7 integrin** causes an activation of the c-Raf-1/mitogen-activated protein (MAP) 2 kinase signal transduction pathway in muscle cells. The obsd. activation of c-Raf-1/MAP2 kinases is a specific effect, because the **.alpha. 7 integrin** deficiency does not cause unspecific stress as detd. by measurement of the Hsp72/73 level and activity of the JNK2 kinase. Because an increased level of activated FAK was found in muscle of **.alpha.7 integrin**-deficient mice, the activation of c-Raf-1 kinase is triggered most likely by an **integrin**-dependent pathway. In accordance with this, in the **integrin .alpha.7**-deficient mice, part of the **integrin** .beta.1D variant in muscle is replaced by the .beta.1A variant, which permits the FAK activation. A recent report describes that **integrin** activity can be down-modulated by the c-Raf-1/MAP2 kinase pathway. Specific activation of the c-Raf-1/MAP2 kinases by cell-permeable peptides in skeletal muscle of rabbits causes degeneration of muscle fibers. Therefore, we conclude that in **.alpha. 7 integrin**-deficient mice, the continuous activation of c-Raf-1 kinase causes a permanent redn. of **integrin** activity diminishing **integrin**-dependent cell-matrix interactions and thereby contributing to the development of the **dystrophic** phenotype.
ST cRaf1 kinase signal transduction **integrin** deficiency muscle **dystrophy**
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PreS1/PreS2; **.alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**
IT **Muscle, disease**
(degeneration; **.alpha.7 integrin** deficiency causes an activation of c-Raf-1 mitogen-activated protein 2

kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**.

IT CD antigens
CD antigens
Integrins
Integrins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**integrin .alpha.7; .alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p125FAK; **.alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)

IT Disease models
Mouse
Muscle
Muscular dystrophy
Signal transduction, biological
(**.alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.beta.1; .alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)

IT 139691-76-2, c-Raf-1 kinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)

IT 141467-21-2
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.alpha.7 integrin** deficiency causes an activation of c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)

IT 144114-16-4, Focal adhesion kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**.alpha.7 integrin** deficiency causes an activation of c-Raf-1 mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**

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L36 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:296448 HCAPLUS
DN 131:71843
TI Laminin polymerization induces a receptor-cytoskeleton network
AU Colognato, Holly; Winkelmann, Donald A.; Yurchenco, Peter D.
CS Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Piscataway, NJ, 08854, USA
SO Journal of Cell Biology (1999), 145(3), 619-631
CODEN: JCLBA3; ISSN: 0021-9525
PB Rockefeller University Press
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry
Section cross-reference(s): 14
AB The transition of laminin from a monomeric to a polymd. state is thought to be a crucial step in the development of basement membranes and in the case of skeletal muscle, mutations in laminin can result in severe **muscular dystrophies** with basement membrane defects. We have evaluated laminin polymer and receptor interactions to det. the requirements for laminin assembly on a cell surface and investigated what cellular responses might be mediated by this transition. We found that on muscle cell surfaces, laminins preferentially polymerize while bound to receptors that included dystroglycan and **.alpha.7. beta.1 integrin**. These receptor interactions are mediated through laminin COOH-terminal domains that are spatially and functionally distinct from NH2-terminal polymer binding sites. This receptor-facilitated self-assembly drives rearrangement of laminin into a cell-assocd. polygonal network, a process that also requires actin reorganization and tyrosine phosphorylation. As a result, dystroglycan and **integrin** redistribute into a reciprocal network as do cortical cytoskeletin components vinculin and **dystrophin**. Cytoskeletal and receptor reorganization is dependent on laminin polymn. and fails in response to receptor occupancy alone. Nonpolymg. laminin. Preferential polymn. of laminin on cell surfaces, and the resulting induction of cortical architecture, is a cooperative process requiring laminin-receptor ligation, receptor-facilitated self-assembly, actin reorganization, and signaling events.
ST laminin polymn **integrin** dystroglycan cytoskeletin basement

membrane **muscular dystrophy**

IT **Muscular dystrophy**
(implications of laminin polymn. induction of receptor-cytoskeleton network in)

IT Actins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(laminin polymn. induces receptor-actin cytoskeleton network)

IT Cytoskeleton
Molecular association
Polymerization
(laminin polymn. induces receptor-cytoskeleton network)

IT Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(laminin polymn. induces receptor-cytoskeleton network)

IT **Dystrophin**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(laminin polymn. induces receptor-cytoskeleton network contg.)

IT Vinculin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(laminin polymn. induces receptor-cytoskeleton network contg.)

IT **Basement membrane**
Muscle
(laminin polymn. induces receptor-cytoskeleton network in)

IT **Muscle**
(myotubule; laminin polymn. induces receptor-cytoskeleton network in)

IT Phosphorylation, biological
(protein; laminin polymn. induces receptor-cytoskeleton network involving tyrosine)

IT Cell membrane
(sarcolemma; laminin polymn. induces receptor-cytoskeleton network on)

IT Glycoproteins, specific or class
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha.-dystroglycans; laminin polymn. induces receptor-cytoskeleton network contg.)

IT **Integrins**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.alpha.7.beta.1**; laminin polymn. induces receptor-cytoskeleton network contg.)

IT 60-18-4, L-Tyrosine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(laminin polymn. induces receptor-cytoskeleton network involving phosphorylation of)

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L36 ANSWER [illegible] OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:621913 HCAPLUS
DN 131:168749

TI Secondary reduction of .alpha.7B **integrin** in laminin .alpha.2 deficient congenital **muscular dystrophy** supports an additional transmembrane link in skeletal muscle

AU Cohn, Ronald D.; Mayer, Ulrike; Saher, Gesine; Herrmann, Ralf; van der Flier, Arjan; Sonnenberg, Arnoud; Sorokin, Lydia; Voit, Thomas

CS Departments of Pediatrics and Pediatric Neurology, University of Essen, Essen, 45122, Germany

SO Journal of the Neurological Sciences (1999), 163(2), 140-152
CODEN: JNSCAG; ISSN: 0022-510X

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

CC 14-11 (Mammalian Pathological Biochemistry)

AB The **integrins** are a large family of heterodimeric transmembrane cellular receptors which mediate the assocn. between the extracellular matrix (ECM) and cytoskeletal proteins. The .**alpha.7**.**beta.1 integrin** is a major laminin binding **integrin** in skeletal and cardiac muscle and is thought to be involved in myogenic differentiation and migration processes. The main binding partners of the .**alpha.7 integrin** are laminin-1 (.alpha.1-.**beta.1**-.gamma.1), laminin-2 (.alpha.2-.**beta.1**-.gamma.1) and laminin-4 (.alpha.2-.beta.1-.gamma.1). Targeted deletion of the gene for the .**alpha.7 integrin** subunit (ITGA7) in mice leads to a novel form of **muscular dystrophy**. In the present study we have investigated the expression of two alternative splice variants, the .**alpha.7B** and .beta.1D **integrin** subunits, in normal human skeletal muscle, as well as in various forms of **muscular dystrophy**. In normal human skeletal muscle the expression of the .**alpha.7 integrin** subunit appeared to be developmentally regulated: it was first detected at 2 yr of age. In contrast, the .beta.1D **integrin** could be detected in immature and mature muscle in the sarcolemma of normal fetal skeletal muscle at 13 wk gestation. The expression of .**alpha.7B integrin** was significantly reduced at the sarcolemma in six patients with laminin .alpha.2 chain deficient congenital **muscular dystrophy** (CMD) (age >2 yr). However, this redn. was not correlated with the amt. of laminin .alpha.2 chain expressed. In contrast, the expression of the laminin .alpha.2 chain was not altered in the skeletal muscle of the .**alpha.7** knock-out mice. These data arguing in favor that there is not a tight correlation between the expression of the .**alpha.7 integrin** subunit and that of the laminin .alpha.2 chain in either human or murine **dystrophic** muscle. Interestingly, in **dystrophinopathies** (Duchenne and Becker **muscular dystrophy**; DMD/BMD) expression of .**alpha.7B** was upregulated irresp. of the level of **dystrophin** expression as shown by a strong sarcolemmal staining pattern even in young boys (age <2 yr). The expression of the .beta.1D **integrin** subunit was not altered in any of our patients with different types of **muscular dystrophy**. In contrast, sarcolemmal expression of .beta.1D **integrin** was significantly reduced in the .**alpha.7 integrin** knock-out mice, whereas the expression of the components of the DGC was not altered. The secondary loss of .**alpha.7B** in laminin .alpha.2 chain deficiency defines a biochem. change in the compn. of the plasma membrane resulting from a primary protein deficiency in the basal lamina. These findings, in addn. to the occurrence of a **muscular dystrophy** in .**alpha.7** deficient mice, implies that the .**alpha.7B integrin** is an important laminin receptor within the plasma membrane which plays a significant role in skeletal muscle function and stability.

ST **alpha7B integrin** laminin alpha1 muscle

dystrophy
IT Muscular dystrophy
(Duchenne and Becker; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Disease, animal
(deficiency, laminin.alpha.2 chain; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Muscular dystrophy
(laminin .alpha.2 chain deficient congenital; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Cell membrane
(sarcolemma; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice
IT Muscle
(secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Dystrophin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Laminins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.alpha.2 chain deficiency; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Laminin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.7B integrin is a; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Integrins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha.7B1; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice)
IT Integrins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.beta.1D; secondary redn. of .alpha.7B integrin in laminin .alpha.2 deficient congenital muscular dystrophy skeletal muscle in humans and in mice
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
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2 Bao, J; J Cell Sci 1999, V112, P865 MEDLINE

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L36 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:191122 HCAPLUS
DN 131:127849
TI The **.alpha.7.beta.1**
integrin in muscle development and disease
AU Burkin, Dean J.; **Kaufman, S. J.**
CS Department of Cell and Structural Biology, University of Illinois, B107 Chemical and Life Sciences Laboratory, Urbana, IL, 61801, USA
SO Cell & Tissue Research (1999), 296(1), 183-190
CODEN: CTSRCS; ISSN: 0302-766X
PB Springer-Verlag

DT Journal; General Review
LA English
CC 13-3 Mammalian Biochemistry
Section cross-reference(s): 14
AB A review, with 43 refs. The **.alpha.7.beta.1 integrin** is a laminin receptor on the surface of skeletal myoblasts and myofibers. Alternative forms of both the **.alpha.7** and **.beta.1** chains are expressed in a developmentally regulated fashion during myogenesis. These different **.alpha.7.beta.1** isoforms localize at specific sites on myofibers and appear to have distinct functions in skeletal muscle. These functions include the migration and proliferation of developing myoblasts, the formation and integrity of neuromuscular and myotendinous junctions, and the "gluing" together of muscle fibers that is essential to the generation of contractile force. The **.alpha.7.beta.1 integrin** appears to be both directly and indirectly causally related to several muscle diseases. Enhanced expression of **.alpha.7.beta.1**-mediated linkage of the extracellular matrix is seen in Duchenne **muscular dystrophy** and may compensate for the absence of the **dystrophin**-mediated linkage. Downregulation of expression of the **integrin** may contribute to the development of pathol. in congenital laminin deficiencies. Mutations in the **.alpha.7 integrin** gene underlie addnl. congenital muscle diseases. The functional roles of this **integrin** in the formation and stability of the neuromuscular and myotendinous junctions and its localization between fibers suggest that altered expression or function of this **integrin** may have widespread involvement in other myopathies. The localization of the **.alpha.7** gene at human chromosome 12q13 is a useful clue for focusing such studies.
ST review **integrin** muscle development disease
IT Development, mammalian postnatal
Muscle
Muscle, disease
(**.alpha.7.beta.1 integrin** in muscle development and disease)
IT **Integrins**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**.alpha.7.beta.1**; **.alpha.7.beta.1 integrin** in muscle development and disease)
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L66 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:670188 HCAPLUS
DN 129:271470
TI The expression of the **alpha**(7)**beta**(1) **integrin** in skeletal muscle development and **muscular dystrophy**
AU Hodges, Bradley Lowell
CS Univ. of Illinois, Urbana, IL, USA
SO (1998) 107 pp. Avail.: UMI, Order No. DA9834690
From: Diss. Abstr. Int., B 1998, 59(5), 2030
DT Dissertation
LA English
CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 13, 14
AB Unavailable
ST **integrin** gene expression skeletal muscle development; **muscular dystrophy integrin** expression
IT RNA splicing
(alternative, .**alpha**.7.**beta**.1 **integrin**; expression of the **alpha**(7) **beta**(1) **integrin** in skeletal muscle development and **muscular dystrophy**)
IT **Muscle**
Muscular dystrophy
(expression of the **alpha**(7 **beta**(1) **integrin** in skeletal muscle development and **muscular dystrophy**)
IT Gene
(expression, .**alpha**.7.**beta**.1 **integrin**; expression of the **alpha** 7 **beta** 1 **integrin** in skeletal muscle development and **muscular dystrophy**
IT Development, mammalian postnatal
myogenesis; expression of the **alpha** 7 **beta** 1 **integrin** in skeletal muscle development and **muscular dystrophy**

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**.alpha.7.beta.1**; expression of the **alpha7beta1 integrin** in skeletal muscle development and **muscular dystrophy**)

L36 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:808972 HCAPLUS
DN 128:100696
TI Altered expression of the **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**
AU Hodges, B. L.; Hayashi, Y. K.; Nonaka, I.; Wang, W.; Arahata, K.; **Kaufman, S. J.**
CS Department of Cell and Structural Biology, University of Illinois, Urbana, IL, USA
SO Journal of Cell Science (1997), 110(22), 2873-2881
CODEN: JNCSAI; ISSN: 0021-9533
PB Company of Biologists Ltd.
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB The **.alpha.7.beta.1 integrin** is the primary laminin receptor on skeletal myoblasts and adult myofibers. It has distinct functions during muscle development and contributes to muscle structural integrity. The authors have studied this **integrin** in cases where expression of **dystrophin** or laminin are compromised. Immunofluorescence demonstrates an increase in **.alpha.7.beta.1** in patients with Duchenne **muscular dystrophy** and in mdx mice that lack **dystrophin**. Anal. of RNA from mdx mice and from patients with Duchenne and Becker **muscular dystrophies** indicates that the increase in the **.alpha.7.beta.1 integrin** is regulated at the level of **.alpha.7** gene transcription. In contrast, the levels of **alpha.7.beta.1 integrin** are severely diminished in patients with laminin .alpha.2 chain congenital **dystrophy muscular dystrophy** and in dy/dy mice that also do not make the .alpha.2 laminin chain. Anal. of RNA from the hindlimbs of dy/dy mice demonstrated that in the absence of laminin, **alpha.7** gene transcription is inhibited and limited to specific alternatively spliced isoforms. The authors suggest that the increased expression of **.alpha.7.beta.1 integrin** in the absence of **dystrophin** compensates for the reduced **dystrophin**-mediated linkage of fibers with the basal lamina and modulates the development of pathol. assocd. with these diseases. The decrease in **.alpha.7.beta.1 integrin** and its transcripts in the absence of laminin likely contributes to the severe myopathy that results from laminin .alpha.2 chain deficiency and suggests that laminin-4 regulates expression of the **.alpha.7 integrin** gene. The role of the **.alpha.7.beta.1 integrin** in muscle integrity also suggests that compromised expression of this receptor may underlie as yet undefined myopathies.
ST **alpha7beta1 integrin** altered expression **muscular dystrophy**; gene expression **alpha7beta1 integrin muscular dystrophy**
IT Laminins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological occurrence);

BSU (Biological study, unclassified ; BIOL (Biological study ; OCCU (Occurrence)
; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies** in relation to)

IT **Muscular dystrophy**
(Becker's; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**

IT **Muscular dystrophy**
(**Duchenne**; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**)

IT mRNA
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation ; BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**)

IT **Dystrophin**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies** in relation to)

IT **Basement membrane**
(basal lamina; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies** in relation to)

IT **Muscular dystrophy**
(**congenital**, merosin-deficient; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**)

IT Mouse
(dy/dy and mdx; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**)

IT Gene
(expression; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**)

IT CD antigens
CD antigens
Integrins
Integrins
RL: ADV (Adverse effect, including toxicity ; BOC (Biological occurrence ; BPR (Biological process); BSU (Biological study, unclassified ; BIOL (Biological study ; OCCU (Occurrence ; PROC (Process
integrin .alpha.7; altered expression of **.alpha.7.beta.1 integrin** in human and murine **muscular dystrophies**

IT RNA splicing
(messenger; altered expression of **.alpha.7**

.beta.1 integrin in human and murine muscular dystrophies in relation to)

IT Transcription, genetic
(regulation; altered expression of .alpha.7 .beta.1 integrin in human and murine muscular dystrophies)

IT Pre-mRNA
RL: BPF (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(splicing; altered expression of .alpha.7 .beta.1 integrin in human and murine muscular dystrophies in relation to)

IT Integrins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha.7.beta.1; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies)

L36 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:700715 HCAPLUS
DN 128:12332
TI Absence of integrin .alpha.7 causes a novel form of muscular dystrophy
AU Mayer, Ulrike; Saher, Gesine; Fassler, Reinhard; Bornemann, Antje; Echtermeyer, Frank; von der Mark, Helga; Miosge, Nicolai; Poschl, Ernst; von der Mark, Klaus
CS Max-Planck-Inst. Biochem., Martinisried, D-82152, Germany
SO Nature Genetics (1997), 17(3), 318-323
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB Integrin .alpha.7.beta.1 is a specific cellular receptor for the basement membrane protein laminin-1, as well as for the laminin isoforms -2 and -4. The .alpha.7 subunit is expressed mainly in skeletal and cardiac muscle and has been suggested to be involved in differentiation and migration processes during myogenesis. Three cytoplasmic and two extracellular splice variants that have been described are developmentally regulated and expressed in different sites in the muscle. In adult muscle, the .alpha.7A and .alpha.7B subunits are concd. in myotendinous junctions and along the sarcolemmal membrane. To study the potential involvement of .alpha.7 integrin during myogenesis a null allele of the .alpha.7 gene (itga7) in the germline of mice by homologous recombination in embryonic stem (ES) cells. Surprisingly, mice homozygous for the mutation are viable and fertile, indicating that the .alpha.7.beta.1 integrin is not essential for myogenesis. However, histol. anal. of skeletal muscle revealed typical symptoms of a progressive muscular dystrophy starting soon after birth, but with a distinct variability in different muscle types. The obsd. histopathol. changes strongly indicate an impairment of function of the myotendinous junctions. These findings demonstrate that .alpha.7.beta.1 integrin represents an indispensable linkage between the muscle fiber and the extracellular matrix that is independent of the dystrophin-dystroglycan complex-mediated interaction of the cytoskeleton with the muscle basement membrane.

IT **integrin alpha7 deficiency muscular dystrophy**
IT Alleles
Basement membrane
Extracellular matrix
Fertility
Heart
Muscle
(absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT Disease, animal
(deficiency, **integrin .alpha.7**; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT CD antigens
CD antigens
Integrins
Integrins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**integrin .alpha.7**; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(itga7; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT **Muscle**
Muscle
Tendon
Tendon
(muscle-tendon junction; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT Mutation
(null; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT **Muscular dystrophy**
(progressive; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT Cell membrane
(sarcolemma; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile)
IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
.alpha.7.beta.1; absence of **integrin .alpha.7** causes novel form of progressive **muscular dystrophy** although muscle development is normal and mice are fertile

L24 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:659210 HCAPLUS
DN 127:329552
TI **Integrins** .alpha.7.beta.1 in muscle function and survival: disrupted expression in merosin-deficient congenital **muscular dystrophy**
AU Vachon, Pierre H.; Xu, Hong; Liu, Ling; Loechel, Frosty; Hayashi, Yukiko; Arahata, Kiichi; Reed, John C.; Wewer, Ulla M.; Engvall, Eva
CS La Jolla Cancer Research Center, The Burnham Institute, La Jolla, CA, 92037, USA
SO Journal of Clinical Investigation (1997), 100(7), 1870-1881
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
CC 14-11 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13
AB Mutations in genes coding for **dystrophin**, for .alpha., .beta., .gamma., and .delta.-sarcoglycans, or for the .alpha.2 chain of the basement membrane component merosin (laminin-2/4) cause various forms of **muscular dystrophy**. Analyses of **integrins** showed an abnormal expression and localization of .**alpha.**7.**beta.1** isoforms in myofibers of merosin-deficient human patients and mice, but not in **dystrophin**-deficient or sarcoglycan-deficient humans and animals. It was shown previously that skeletal muscle fibers require merosin for survival and function. Correction of merosin deficiency in vitro through cell transfection with the merosin .alpha.2 chain restored the normal localization of .**alpha.**7.beta.1D **integrins** as well as myotube survival. Overexpression of the apoptosis-suppressing mol. Bcl-2 also promoted the survival of merosin-deficient myotubes, but did not restore a normal expression of .**alpha.**7.beta.1D **integrins**. Blocking of .**beta.1** **integrins** in normal myotubes induced apoptosis and severely reduced their survival. These findings (a) identify .**alpha.**7.beta.1D **integrins** as the de facto receptors for merosin in skeletal muscle; (b) indicate a merosin dependence for the accurate expression and membrane localization of .**alpha.**7.beta.1D **integrins** in myofibers; (c) provide a mol. basis for the crit. role of merosin in myofiber survival; and (d) add new insights to the pathogenesis of neuromuscular disorders.
ST **integrin alpha7beta1** merosin deficiency **muscular dystrophy**; muscle survival **integrin alpha7beta1** merosin deficiency
IT Laminins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(2, deficiency; **integrins** (.**alpha.**7.**beta.1**) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Bcl-2, apoptosis suppression by; **integrins** .**alpha.**7.**beta.1** in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice in relation to
IT **Muscular dystrophy**
congenital, merosin-deficient; **integrins** .**alpha.**7.**beta.1** in muscle function and survival and disrupted expression in merosin-deficient

congenital **muscular dystrophy** in humans and mice)

IT Disease, animal
(deficiency, merosin; **integrins** (.alpha.7 .beta.1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT **Muscle**
(fiber; **integrins** (.alpha.7.beta. 1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT CD antigens
CD antigens
Integrins
Integrins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**integrin** .alpha.7, A and B isoforms; **integrins** (.alpha.7.beta. 1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT Mutation
(**integrins** (.alpha.7.beta. 1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**integrins** (.alpha.7.beta. 1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT Apoptosis
(**integrins** (.alpha.7.beta. 1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice in relation to)

IT Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(merosin, **integrin** .alpha.7.beta.1D as; **integrins** (.alpha.7.beta. 1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.alpha.7.beta.1D; **integrins** (.alpha.7.beta.1) in muscle function and survival and disrupted expression in merosin-deficient congenital **muscular dystrophy** in humans and mice)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

.beta.1, D isoform; **integrins**
.alpha.7.beta.1 in muscle
function and survival and disrupted expression in merosin-deficient
congenital **muscular dystrophy** in humans and mice

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L52 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:352792 BIOSIS
DN PREV200200352792
TI **Integrin alpha7beta1** in **muscular dystrophy**/myopathy of unknown etiology.
AU Pegoraro, Elena (1); Depollaro, Fulvio; Prandini, Paola; Marin, Alessandra; Fanin, Marina; Trevisan, Carlo P.; El-Messlemani, Abdul Hassib; Tarone, Guido; Engvall, Eva; Hoffman, Eric P.; Angelini, Corrado
CS (1) Neuromuscular Center, Department of Neurological and Psychiatric Sciences, University of Padova, 35128, Padova: elena.pegoraro@unipd.it Italy
SO American Journal of Pathology, (June, 2002) Vol. 160, No. 6, pp. 2135-2143. http://ajp.amjpathol.org/. print.
ISSN: 0002-9440.
DT Article
LA English
AB To investigate the role of **integrin alpha7** in muscle pathology, we used a "candidate gene" approach in a large cohort of **muscular dystrophy**/myopathy patients. Antibodies against the intracellular domain of the **integrin alpha7A** and **alpha7B** were used to stain muscle biopsies from 210 patients with **muscular dystrophy**/myopathy of unknown etiology. Levels of **alpha7A** and **alpha7B integrin** were found to be decreased in 35 of 210 patients (approx17%). In six of these patients no **integrin alpha7B** was detected. Screening for **alpha7B** mutation in 30 of 35 patients detected only one **integrin alpha7** missense mutation (the mutation on the second allele was not found) in a patient presenting with a congenital **muscular dystrophy**-like phenotype. No **integrin alpha7** gene mutations were identified in all of the other patients showing **integrin alpha7** deficiency. In the process of mutation analysis, we identified a novel **integrin alpha7** isoform presenting 72-bp deletion. This isoform results from a partial deletion of exon 21 due to the use of a cryptic splice site generated by a G to A missense mutation at nucleotide position 2644 in **integrin alpha7** cDNA. This spliced isoform is present in about 12% of the chromosomes studied. We conclude that secondary **integrin alpha7** deficiency is rather common in **muscular dystrophy**/myopathy of unknown etiology, emphasizing the multiple mechanisms that may modulate **integrin** function and stability.
CC Cytology and Cytochemistry - General [illegible]
Cytology and Cytochemistry - Human [illegible]
Genetics and Cytogenetics - General [illegible]
Genetics and Cytogenetics - Human [illegible]
Pathology, General and Miscellaneous - General [illegible]
Metabolism - Metabolic disorders [illegible]

Muscle - Pathology
Bones, Joints, Fascias, Connective and Adipose Tissue - Pathology
Nervous System - Pathology
BT Hominidae
IT Major Concepts
Cell Biology; Molecular Genetics; Biochemistry and Molecular Biophysics; Neurology (Human Medicine, Medical Sciences); Orthopedics (Human Medicine, Medical Sciences); Pathology
IT Diseases
muscular dystrophy: myopathy of unknown etiology: etiology, genetics, muscle disease, nervous system disease, pathology; secondary **integrin alpha-7** deficiency: complications, metabolic disease, pathology
IT Chemicals & Biochemicals
integrin alpha-7-beta-1: function, stability
IT Methods & Equipment
mutation analysis: genetic method
IT Miscellaneous Descriptors
phenotype
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
GEN human **integrin alpha-7** gene (Hominidae)

L52 ANSWER 14 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:507438 BIOSIS
DN PREV200200507438
TI Expression of **alpha7beta1 integrin** splicing variants during skeletal muscle regeneration.
AU Kaariainen, Minna; Nissinen, Liisa; **Kaufman, Stephen**; Sonnenberg, Arnoud; Jarvinen, Markku; Heino, Jyrki; Kalimo, Hannu (1)
CS (1) Department of Pathology, Turku University Hospital, FIN-20520, Turku: hkalimo@utu.fi Finland
SO American Journal of Pathology, (September, 2002) Vol. 161, No. 3, pp. 1023-1031. http://ajp.amjpathol.org/. print.
ISSN: 0002-9440.
DT Article
LA English
AB **Integrin alpha7beta1** is a laminin receptor, both subunits of which have alternatively spliced, developmentally regulated variants. In skeletal muscle **beta1** has two major splice variants of the intracellular domain (beta1A and beta1D). **alpha7X1** and **alpha7X2** represent variants of the **alpha7** ectodomain, whereas **alpha7A** and **alpha7B** are variants of the intracellular domain. Previously we showed that during early regeneration after transection injury of muscle **alpha7 integrin** mediates dynamic adhesion of myofibers along their lateral aspects to the extracellular matrix. Stable attachment of myofibers to the extracellular matrix occurs during the third week after injury, when new myotendinous junctions develop at the ends of the regenerating myofibers. Now we have analyzed the relative expression of beta1A, beta1D, and **alpha7A** **alpha7B** and **alpha7X1** **alpha7X2** isoforms during regeneration for 4 to 56 days after transection of rat soleus muscle, by reverse transcriptase-polymerase chain reaction and immunohistochemistry. During early regeneration beta1A was the predominant isoform in both muscle and scar tissue. Expression of muscle-specific beta1D was detected in regenerating myofibers from day 4 onwards, i.e., when myogenic nuclear activity began to increase, and it became more abundant with the progression of regeneration. **alpha7B** isoform predominated in day

1. Thereafter, the relative expression of **alpha7A** transcripts increased until day 7 with the concomitant appearance of **alpha7A** immunoreactivity in regenerating myofibers. Finally, **alpha7B** again became the predominant variant in highly regenerated myofibers. Similarly as in the controls, **alpha7X1** and **alpha7X2** isoforms were both expressed throughout the regeneration with a peak in **alpha7X1** expression on day 4 coinciding with the dynamic adhesion stage. The results suggest that during regeneration of skeletal muscle the splicing of **beta1** and **alpha7 integrin** subunits is regulated according to functional requirements. **alpha7A** and **alpha7X1** appear to have a specific role during the dynamic phase of adhesion, whereas **alpha7B**, **alpha7X2**, and beta1D predominate during stable adhesion.

CC   Biochemical Studies - General *10060
     Muscle - Physiology and Biochemistry *17504
BC   Muridae   86375
IT   Major Concepts
       Biochemistry and Molecular Biophysics; Muscular System (Movement and Support)
IT   Parts, Structures, & Systems of Organisms
       skeletal muscle: muscular system, regeneration
IT   Chemicals & Biochemicals
       alpha-7-beta-1 integrin
       splicing variants: expression
ORGN Super Taxa
       Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
       Sprague-Dawley rat (Muridae): adult, male
ORGN Organism Superterms
       Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L52 ANSWER 15 OF 29 BIOSIS
AN   2002:369184 BIOSIS
DN   PREV200200369184
TI   **Integrin**-mediated complementary gene therapy in muscle disease.
AU   Burkin, Dean J. (1); Wallace, Gregory Q. (1); Milner, Derek (1); Chaney, Eric (1); **Kaufman, Stephen J. (1)**
CS   (1) Cell and Structural Biology, University of Illinois, 601 S. Goodwin Ave, Urbana, IL, 61801 USA
SO   FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A726.
     http://www.fasebj.org/. print.
     Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
     ISSN: 0892-6638.
DT   Conference
LA   English
AB   The molecular continuity between the extracellular matrix and cell cytoskeleton is essential for the structural and functional integrity of skeletal and cardiac muscle. Muscle fibers attach to laminin in the basal lamina using two distinct linkage systems, the dystrophin glycoprotein complex and the **alpha7beta1 integrin**. Mutations in the dystrophin gene that result in an absence of the dystrophin protein cause Duchenne **Muscular Dystrophy** (DMD) and affect 1/3,500 newborn males. To test whether elevated levels of the **alpha7 integrin** can compensate for the absence of dystrophin, we expressed the rat **alpha7** chain in mdx/utr (-/-) mice that lack both dystrophin and utrophin. These mice develop a severe **muscular dystrophy** highly akin to DMD and die prematurely. The transgenic expression of the **alpha7BX2** chain in the mdx/utr (-/-) mice reduced the development of skeletal and cardiac muscle disease and increased the longevity of the mice three-fold. This suggests that complementary gene therapy, based on the enhanced expression of the

alpha7beta1 integrin, may provide a novel approach to treat DMD.
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *10501
Genetics and Cytogenetics - Human *13506
Biochemical Studies - Proteins, Peptides and Amino Acids *11064
Muscle - Physiology and Biochemistry *17504
Muscle - Pathology *17506
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
BC Hominidae 86215
Muridae 86375
IT Major Concepts
Medical Genetics (Allied Medical Sciences); Orthopedics (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
skeletal muscle: differentiation, muscular system
IT Diseases
Duchenne muscle dystrophy: muscle disease, therapy
IT Chemicals & Biochemicals
alpha-7-beta-1 integrin
; dystrophin; utrophin
IT Methods & Equipment
integrin-mediated complementary gene therapy: gene therapy method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae); mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
GEN human dystrophin gene (Hominidae): mutations

L52 ANSWER 16 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2003:166691 BIOSIS
DN PREV200300166691
TI **Integrin** is a compensatory transmembrane linkage to sarcoglycan in muscle.
AU Allikian, M. J. (1); Hack, A. A. (1); Mewborn, S. (1); Meyer, U.; McNally, E. M. (1)
CS (1) Medicine, University of Chicago, Chicago, IL, USA USA
SO Molecular Biology of the Cell, (Nov. 2002, 2002) Vol. 13, No. Supplement, pp. 318a. print.
Meeting Info.: 42nd Annual Meeting of the American Society for Cell Biology San Francisco, CA, USA December 14-18, 2002 American Society for Cell Biology
. ISSN: 1059-1524.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *10501
Biochemical Studies - General *11060
Biochemical Studies - Proteins, Peptides and Amino Acids *11064
Cardiovascular System - Heart Pathology *14516
Muscle - Physiology and Biochemistry *17504
Muscle - Pathology *17506
Nervous System - Pathology *21516
BC Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Muscular System Movement and

Support)
IT Parts, Structures, & Systems of Organisms
muscle: muscular system; plasma membrane
IT Diseases
cardiomyopathy: heart disease; **muscular dystrophy**: muscle disease, nervous system disease
IT Chemicals & Biochemicals
dystroglycan; dystrophin; gamma-sarcoglycan; **integrin**: compensatory transmembrane linkage; **integrin-alpha-7-beta-1**; myosin heavy chain; sarcoglycan
IT Alternate Indexing
Cardiomyopathy, Congestive (MeSH); **Muscular Dystrophies** (MeSH)
IT Methods & Equipment
histologic examination: histology and cytology techniques, laboratory techniques; immunostaining: immunologic techniques, laboratory techniques
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 153-37-7 (**INTEGRIN**)
80791-49-0 (**INTEGRIN**)

L52 ANSWER 17 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:355320 BIOSIS
DN PREV200200355320
TI **Integrin alpha7beta1** in **muscular dystrophy** myopathy of unknown etiology.
AU Pegoraro, Elena (1); Prandini, Paola (1); Fanin, Marina (1); Tarone, Guido; Engvall, Eva; Angelini, Corrado (1)
CS (1) Padova Italy
SO Neurology, (April 9, 2002) Vol. 58, No. 7 Supplement 3, pp. A316. http://www.neurology.org/. print.
Meeting Info.: 54th Annual Meeting of the American Academy of Neurology Denver, Colorado, USA April 13-20, 2002
ISSN: 0028-3878.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Human *03508
Pathology, General and Miscellaneous - Diagnostic *12504
Muscle - Physiology and Biochemistry *17504
Muscle - Pathology *17506
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18014
Nervous System - Pathology *21006
EC Hominidae *80115
IT Major Concepts
Medical Genetics (Allied Medical Sciences); Orthopedics (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
muscle: muscular system
IT Diseases
muscular dystrophy: etiology, genetics, muscle disease, nervous system disease; myopathy: etiology, genetics, muscle disease

IT Chemicals & Biochemicals
integrin alpha-7: intracellular domain
IT Alternate Indexing
Muscular Dystrophy (MeSH)
IT Methods & Equipment
muscle biopsy: diagnostic method
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
GEN human **integrin alpha-7** gene (Hominidae):
missense mutations

L52 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:427550 BIOSIS
DN PREV200200427550
TI Localization of **alpha7 integrins** and dystrophin suggests potential for both lateral and longitudinal transmission of tension in large mammalian muscles.
AU Paul, Angelika C.; Sheard, Philip W.; **Kaufman, Stephen J.**; Duxson, Marilyn J. (1)
CS (1) Department of Anatomy and Structural Biology, University of Otago, PO Box 913, Dunedin, 9001: marilyn.duxson@stonebow.otago.ac.nz New Zealand
SO Cell & Tissue Research, (May, 2002) Vol. 308, No. 2, pp. 255-265. print. ISSN: 0302-766X.
DT Article
LA English
AB Non-primate mammalian muscles with fascicles above 35 mm in length are composed predominantly of arrays of short, non-spanning muscle fibres, which terminate within the belly of the muscle fascicle at one or both ends. We have previously described the morphological form of various muscle-to-muscle and muscle-to-matrix junctions which are likely involved in tension transmission within one such muscle - the guinea pig sternomastoid muscle (Young et al. 2000). Here, we use immunohistochemistry to investigate the cell adhesion molecules present at these junctions. We find strong immunoreactivity against the **alpha7B integrin** subunit and dystrophin, and slight reactivity against the **alpha7A integrin** at all intrafascicular fibre terminations (IFTs), as well as at the muscle-tendon junction (MTJ). Tenascin, the sole ligand for alpha7beta1 **integrin**, was absent from IFTs but present at the MTJ, suggesting the two sites are molecularly distinct. In addition to their expression at junctional sites, **alpha7B integrin** and dystrophin were also expressed ubiquitously along the non-junctional sarcolemma, suggesting potential involvement in diffuse lateral transmission of tension between adjacent fibres. We conclude that the distribution of **alpha7beta1 integrins** and dystrophin in series-fibred muscles suggests they are involved in transmission of tension from intrafascicularly terminating fibres to neighbouring fibres lying both in-series and in-parallel, via the extracellular matrix (ECM).
CC Biochemical Studies - Proteins, Peptides and Amino Acids (10064)
Muscle - Physiology and Biochemistry (17514)
BC Cavildae (06001)
Muridae (06075)
IT Major Concepts
Muscular System: Movement and Support
IT Parts, Structures, & Systems of Organisms
anterior gracilis muscle: muscular system; sternomastoid muscle: muscular system

IT Chemicals & Biochemicals
alpha-7 integrins: large mammalian muscle localization, lateral tension transmission role, longitudinal tension transmission role; dystrophin: large mammalian muscle localization, lateral tension transmission role, longitudinal tension transmission role
ORGN Super Taxa
Caviidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
guinea pig (Caviidae): animal model; rat (Muridae): animal model
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L52 ANSWER 19 OF 29 BIOSIS
AN 2000:460479 BIOSIS
DN PREV200000460479
TI Laminin and **alpha7beta1 integrin** regulate agrin-induced clustering of acetylcholine receptors.
AU Burkin, Dean J.; Kim, Jae Eun; Gu, Maojian; **Kaufman, Stephen J. (1)**
CS (1) Department of Cell and Structural Biology, University of Illinois, Urbana, IL, 61801 USA
SO Journal of Cell Science, (August, 2000) Vol. 113, No. 16, pp. 2877-2886. print.
ISSN: 0021-9533.
DT Article
LA English
SL English
AB The clustering of acetylcholine receptors (AChRs) in the post-synaptic membrane of skeletal muscle is an early developmental event in the formation of the neuromuscular junction. Several studies show that laminin, as well as neural agrin, can induce AChR clustering in C2C12 myofibers. We recently showed that specific isoforms of the **alpha7beta1 integrin** (a receptor normally found at neuromuscular junctions) colocalize and physically interact with AChR clusters in a laminin-dependent fashion. In contrast, induction with agrin alone fails to promote localization of the **integrin** with AChR clusters. Together both agrin and laminin enhance the interaction of the **integrin** with AChRs and their aggregation into clusters. To further understand this mechanism we investigated cluster formation and the association of the **alpha7beta1 integrin** and AChR over time following induction with laminin and/or agrin. Our results show that the **alpha7beta1 integrin** associates with AChRs early during the formation of the post-synaptic membrane and that laminin modulates this recruitment. Laminin induces a rapid stable association of the **integrin** and AChRs and this association is independent of clustering. In addition to laminin-1, merosin (laminin-2/4) is present both before and after formation of neuromuscular junctions and also promotes AChR clustering and colocalization with the **integrin** as well as synergism with agrin. Using site directed mutagenesis we demonstrate that a tyrosine residue in the cytoplasmic domain of both **alpha7A** and **alpha7B** chains regulates the localization of the **integrin** with AChR clusters. We also provide evidence that laminin, through its association with the **alpha7beta1 integrin**, reduces by 20-fold the concentration of agrin required to promote AChR clustering and accelerates the formation of clusters. Thus laminin, agrin and the **alpha7beta1 integrin** act in a concerted manner early in the development of the post-synaptic membrane, with laminin priming newly formed myofibers to rapidly and vigorously respond to low concentrations of neural agrin produced by innervating motor neurons.

CC Cytology and Cytochemistry - Animal *02810
Biochemical Studies - Proteins, Peptides and Amino Acids *10504
Muscle - Physiology and Biochemistry *17504
Nervous System - Physiology and Biochemistry *20504
IT Major Concepts
Muscular System (Movement and Support); Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
motor neurons: nervous system; myofiber: muscular system; neuromuscular junction: formation, nervous system; post-synaptic membrane: formation, nervous system
IT Chemicals & Biochemicals
acetylcholine receptors [AChRs]: cluster formation, localization; agrin; **alpha-7-A chain**: tyrosine residue; **alpha-7-B chain**; **alpha-7-beta-1 integrin**: localization, regulation; laminin-1; merosin [laminin-2/4]; tyrosine
RN 60-18-4Q (TYROSINE)
556-03-6Q (TYROSINE)

L52 ANSWER 20 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:60768 BIOSIS
DN PREV200000060768
TI Interaction of the **alpha7beta1 integrin** and acetylcholine receptor during formation of the neuromuscular junction.
AU **Kaufman, Stephen J. (1)**; Burkin, Dean J. (1)
CS (1) University of Illinois, 601 S. Goodwin Ave., B107 CLSL, Urbana, IL USA
SO Molecular Biology of the Cell, (Nov., 1999) Vol. 10, No. SUPPL., pp. 353a. Meeting Info.: 39th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 11-15, 1999 The American Society for Cell Biology
. ISSN: 1059-1524.
DT Conference
LA English
CC Biochemical Studies - General *10060
Cytology and Cytochemistry - General *02502
Biophysics - Membrane Phenomena *10508
Nervous System - Physiology and Biochemistry *20504
Muscle - Physiology and Biochemistry *17504
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
IT Major Concepts
Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
acetylcholine receptor; agrin; **alpha-7-beta-1 integrin**; laminin
IT Miscellaneous Descriptors
muscle fiber; neuromuscular junction: formation; Meeting Abstract

L52 ANSWER 21 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:455029 BIOSIS
DN PREV199900455029
TI A functional role for specific isoforms of the **alpha7beta1 integrin** in the early development of acetylcholine receptor clusters.
AU Burkin, D. J. (1); Gu, M. (1); Wallace, G. Q. (1); **Kaufman, S. J. (1)**
CS (1) University of Illinois, Urbana, IL USA
SO Developmental Biology, (June 1, 1999) Vol. 211, No. 1, pp. 248. Meeting Info.: 58th Annual Meeting of the Society for Developmental Biology Charlottesville, Virginia, USA June 11-15, 1999 Society for Developmental Biology

. ISSN: 1012-1616.
DT Conference
LA English
CC Developmental Biology - Embryology - General and Descriptive *10811
Microscopy Techniques - General and Special Techniques *01102
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10302
Nervous System - General; Methods *20501
Muscle - General; Methods *17501
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Mammalia - Unspecified 85700
IT Major Concepts
Biochemistry and Molecular Biophysics; Development; Muscular System (Movement and Support)
IT Parts, Structures, & Systems of Organisms
muscle: muscular system; neuromuscular junction: nervous system
IT Chemicals & Biochemicals
acetylcholine receptor clusters; **alpha7beta1 integrin**
: functional role, isoforms
IT Methods & Equipment
immunofluorescence microscopy: microscopy method; immunoprecipitation: analytical method; Western analysis: analytical method
IT Miscellaneous Descriptors
embryogenesis; Meeting Abstract
ORGN Super Taxa
Mammalia: Vertebrata, Chordata, Animalia
ORGN Organism Name
mammal (Mammalia): embryo
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates
RN 153-87-7 (**INTEGRIN**)
60791-49-1 (**INTEGRIN**)
51-84-3 (ACETYLCHOLINE)

L52 ANSWER 32 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:256802 BIOSIS
DN PREV199800256802
TI Mutations in the **integrin alpha7** gene cause congenital myopathy.
AU Hayashi, Yukiko K.; Chou, Fan-Li; Engvall, Eva; Ogawa, Megumu; Matsuda, Chie; Hirabayashi, Shinichi; Yokochi, Kenji; Ziober, Barry L.; Kramer, Randall H.; **Kaufman, Stephen J.**; Ozawa, Eijiro; Goto, Yu-Ichi; Nonaka, Ikuya; Tsukahara, Toshifumi; Wang, Jian-Zhou; Hoffman, Eric P.; Arahata, Kiichi (1)
CS (1) Dep. Neuromuscular Res., Natl. Inst. Neurosci., Natl. Cent. Neurol. Psychiatry, Kodaira, Tokyo 187-8502 Japan
SO Nature Genetics, (May, 1998) Vol. 18, No. 1, pp. 94-97.
ISSN: 1061-4036.
DT Article
LA English
AB The basal lamina of muscle fibers plays a crucial role in the development and function of skeletal muscle. An important laminin receptor in muscle is **integrin alpha7beta1D. Integrin beta1** is expressed throughout the body, while **integrin alpha7** is more muscle-specific. To address the role of **integrin alpha7** in human muscle disease, we determined **alpha7** protein expression in muscle biopsies from 117 patients with unclassified congenital myopathy and congenital **muscular dystrophy** by immunocytochemistry. We found three unrelated patients with **integrin alpha7** deficiency and normal laminin alpha2 chain expression. To determine if any of these three

patients had mutations of the **integrin alpha7** gene, ITGA7, we cloned and sequenced the full-length human ITGA7 cDNA, and screened the patients for mutations. The patient had splice mutations on both alleles; one causing a 21-bp insertion in the conserved cysteine-rich region, and the other causing a 98-bp deletion. A second patient was a compound heterozygote for the same 98-bp deletion, and had a 1-bp frame-shift deletion on the other allele. A third showed marked deficiency of ITGA7 mRNA. Clinically, these patients showed congenital myopathy with delayed motor milestones. Our results demonstrate that mutations in ITGA7 are involved in a form of congenital myopathy.

CC Genetics and Cytogenetics - Human *03508
Biophysics - General Biophysical Techniques *10804
Enzymes - Methods *10804
Muscle - Pathology *17506
Nervous System - Pathology *20506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
BC Hominidae 86215
IT Major Concepts
Genetics; Muscular System (Movement and Support)
IT Diseases
congenital **muscular dystrophy**: congenital disease, nervous system disease, genetic disease; congenital myopathy: congenital disease, muscle disease
IT Chemicals & Biochemicals
cDNA [complementary DNA]; **integrin alpha-7** gene: mutation; **integrin alpha-7** protein: expression; mRNA [messenger RNA]
IT Methods & Equipment
immunoblotting: analytical method, detection/labeling techniques; immunocytochemistry: analytical method, detection/labeling techniques; RT-PCR [reverse transcriptase-polymerase chain reaction]: amplification method, quantitation method, amplification techniques; SDS-PAGE [SDS-polyacrylamide gel electrophoresis]: electrophoretic techniques, separation method
IT Miscellaneous Descriptors
research
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L52 ANSWER 23 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:456225 BIOSIS
DN PREV199799755428
TI The **alpha-7-beta-1** **integrin** mediates adhesion and migration of skeletal myoblasts on laminin.
AU Crawley, Suzanne; Farrell, Eleanor M.; Wang, Weiywang; Gu, Maojian; Huang, Hui-Yu; Huynh, Vu; Hodges, Bradley L.; Cooper, Douglas N. W. [1]; **Kaufman, Stephen J.**
CS [1] LPPI-Box P-1044, 421 Parnassus Ave., San Francisco, CA 94143 USA
SO Experimental Cell Research, 1997, Vol. 236, No. 1, pp. 274-282. ISSN: 0014-4827.
DT Article
LA English
AB Many aspects of myogenesis are believed to be regulated by myoblast interactions with specific components of the extracellular matrix. For example, laminin has been found to promote adhesion, migration, and proliferation of mammalian myoblasts. Based on affinity chromatography, the **alpha-7-beta-1**

integrin has been presumed to be the major receptor mediating myoblast interactions with laminin. We have prepared a monoclonal antibody, 3C6, that specifically reacts with both the M1 and the M2 extracellular splice variants of the **alpha-7** **integrin** chain. This antibody completely and selectively blocks adhesion and migration of rat L8E63 myoblasts on laminin-1, but not on fibronectin. In contrast, a polyclonal antibody to the fibronectin receptor, alpha-5-**beta-1** **integrin**, blocks myoblast adhesion on fibronectin, but not on laminin-1. The **alpha** **-7-beta-1** **integrin** also binds to a mixture of laminin-2 and laminin-4, the major laminin isoforms in developing and adult skeletal muscle, but 3C6 is a much less potent inhibitor of myoblast adhesion on the laminin-2/4 mixture than on laminin-1. Based on affinity chromatography, we suggest that this may be due to higher affinity binding of alpha-7X1 to laminin-2/4 than to laminin-1.

CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Muscle - Physiology and Biochemistry *17504
In Vitro Studies, Cellular and Subcellular *32600
BC Muridae *86[illegible]
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Membranes (Cell Biology); Muscular System (Movement and Support)
IT Chemicals & Biochemicals
INTEGRIN
IT Miscellaneous Descriptors
ADHESION; **ALPHA-7-BETA-1** **INTEGRIN**; BIOCHEMISTRY AND BIOPHYSICS; CELL BIOLOGY; FIBRONECTIN; LAMININ; L8E63 CELL LINE; MIGRATION; MOUSE MYOBLAST; MUSCULAR SYSTEM; RAT MYOBLASTS; SKELETAL MUSCLE DEVELOPMENT; SKELETAL MYOBLAST
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
C2C12 (Muridae): cell line
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN 153-37-7 (**INTEGRIN**)
60791-44-3 (**INTEGRIN**)

L52 ANSWER 24 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:[illegible] BIOSIS
DN PREV[illegible]
TI Comparison of rat myoblast receptors for laminin-1 and laminin-2/4.
AU Crawley, S. C. (1); **Kaufman, S. J.**; Cooper, D. N. W.
CS (1) Dep. Psychiatry, University California, San Francisco, CA [illegible] USA
SO Molecular Biology of the Cell, (1996) Vol. 7, No. SUPPL., pp. 47A.
Meeting Info.: Annual Meeting of the 4th International Congress on Cell Biology and the 36th American Society for Cell Biology San Francisco, California, USA December [illegible], 1996
ISSN: [illegible].
DT Conference; Abstract; Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals [illegible]
Cytology and Cytochemistry - Animal *[illegible]
Biochemical Studies - General *[illegible]
Biophysics - General Biophysical Studies *[illegible]

BC Muridae *06375
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology
IT Chemicals & Biochemicals
INTEGRIN
IT Miscellaneous Descriptors
ALPHA-7-BETA-1 INTEGRIN
; LAMININ 1; LAMININ 1 RECEPTOR; LAMININ-2/4; LAMININ-2/4 RECEPTOR; MEMBRANES; MYOBLAST
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN 113-87-7Q (**INTEGRIN**)
c'701-43-3Q (**INTEGRIN**)

L52 ANSWER 25 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1994:327133 BIOSIS
DN PREV199497340253
TI Developmental regulation of the structure and function of **alpha-7-beta-1 integrin** in skeletal muscle.
AU Wang, Weigwang; **Kaufman, Stephen J.**
CS Dep. Cell and Structural Biol., Univ. Ill., Urbana, IL 61801 USA
SO Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18D, pp. 312.
Meeting Info.: Keystone Symposium on Molecular Biology of Muscle Development Snowbird, Utah, USA April 11-17, 1994
ISSN: 0733-1959.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines 10052
Biochemical Methods - Proteins, Peptides and Amino Acids 10054
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics - Molecular Properties and Macromolecules 10506
Biophysics - Membrane Phenomena *10508
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Muscle - Physiology and Biochemistry *17504
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Vertebrata - Unspecified *06150
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Development; Genetics; Membranes (Cell Biology); Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics); Muscular System (Movement and Support)
IT Chemicals & Biochemicals
INTEGRIN; ACTIN
IT Miscellaneous Descriptors
ACTIN; FIBRONECTIN; GENE EXPRESSION; LAMININ; MEETING ABSTRACT; MEETING POSTER; RNA
ORGN Super Taxa
Vertebrata - Unspecified: Vertebrata, Chordata, Animalia
ORGN Organism Name

Vertebrata Vertebrata - Unspecified
ORGN Organism Superterms
animals; chordates; nonhuman vertebrates; vertebrates
RN 153-87-7Q (**INTEGRIN**
60791-49-3Q (**INTEGRIN**
132879-21-8 (ACTIN)

L52 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1994:325158 BIOSIS
DN PREV199497338158
TI Developmental regulation of the interaction of **alpha-7 -beta-1 integrin** and extracellular matrix in skeletal muscle.
AU **Kaufman, Stephen J.**; Song, Woo Keun; Sato, Hiro; Wang, Weigwang
CS Dep. Cell and Structural Biol., Univ. Ill., Urbana, IL 61801 USA
SO Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18C, pp. 250.
Meeting Info.: Keystone Symposium on Biology of Physicochemical Interactions at the Cell Surface Taos, New Mexico, USA February 20-26, 1994
ISSN: 0733-1959.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Enzymes - Physiological Studies *10808
Muscle - Physiology and Biochemistry *17504
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Muscular System (Movement and Support)
IT Chemicals & Biochemicals
INTEGRIN
IT Sequence Data
amino acid sequence
IT Miscellaneous Descriptors
FIBRONECTIN; LAMININ; MEETING ABSTRACT; MEETING POSTER; MYOBLASTS; RNA; TYROSINE PHOSPHATASE
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 153-87-7Q (**INTEGRIN**)
60791-49-3Q (**INTEGRIN**)

L52 ANSWER 27 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1994:162130 BIOSIS
DN PREV199497178130
TI Selective modulation of the interaction of **alpha-7-beta-1 integrin** with fibronectin and laminin by L-14 lectin during skeletal muscle differentiation..
AU Gu, Maojian; Wang, Weigwang; Song, Woo Keun; Cooper, Douglas N. W.; **Kaufman, Stephen J. (1)**
CS (1) Dep. Cell Structural Biol., Univ. Illinois, Urbana, IL 61801 USA
SO Journal of Cell Science, (1994) Vol. 107, No. 1, pp. 175-181.
ISSN: 0021-9533.
DT Article

LA English
AB The **alpha-7-beta-1** **integrin** was originally identified and isolated from differentiating skeletal muscle and shown to be a laminin-binding protein (Song et al. (1992) J. Cell Biol. 117, 643-657). Expression of the **alpha-7** gene and protein are developmentally regulated during skeletal muscle differentiation and have been used to identify cells at distinct stages of the myogenic lineage (George-Weinstein et al. (1993) Dev. Biol. 156, 209-229). The lactoside-binding protein L-14 exists as a dimer and has been localized on a variety of cells, in association with extracellular matrix. During myogenesis in vitro, L-14 is synthesized within replicating myoblasts but it is not secreted until these cells commence terminal differentiation and fusion into multinucleate fibers (Cooper and Barondes, J. Cell Biol. (1990) 110, 1681-1691). Addition of purified L-14 to myogenic cells plated on laminin inhibits myoblast spreading and fusion, suggesting that the L-14 lectin regulates muscle cell interactions with the extracellular matrix that are germane to myogenic development (Cooper et al. (1991) J. Cell Biol. 115, 1437-1448). We demonstrate here, using affinity chromatography and immunoblots, that **alpha-7-beta-1** also binds to fibronectin and to the L-14 lectin. L-14 binds to both laminin and to the **alpha-7-beta-1** **integrin**, and it can effectively inhibit the association of laminin and this **integrin**. Modulation of **alpha-7-beta** **-1** interaction with its ligands by L-14 is selective: L-14 does not bind to fibronectin, nor does it interfere with the binding of fibronectin to **alpha-7-beta-1**. These results are discussed in the context of the potential roles of **alpha-7-beta-1** in its interaction with laminin and fibronectin during myogenesis.
CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Muscle - Physiology and Biochemistry *17504
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Development; Muscular System (Movement and Support)
IT Chemicals & Biochemicals
INTEGRIN
IT Miscellaneous Descriptors
EXTRACELLULAR MATRIX; LACTOSIDE BINDING PROTEIN L-14; MYOBLAST; MYOGENESIS; MYOGENIC CELL
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN 153-87-7Q (**INTEGRIN**)
60791-49-3Q (**INTEGRIN**)

L5Z ANSWER 29 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1994:21794 BIOSIS
DN PREV199497033794
TI **Alpha-7-beta-1** **Integrin** is a component of the myotendinous junction on skeletal muscle.
AU Bao, Z. Z. [1]; Lakonishok, M.; **Kaufman, S.**; Horwitz, A. F.
CS [1] Dep. Cell Structural Biol., Univ. Illinois Urbana-Champaign, Urbana, IL 61801 USA
SO Journal of Cell Science, 1993 Vol. 106, No. 2, pp. 579-589.
ISSN: 0021-9533.

DT Article
LA English
AB Immunization against a 71 kDa band that co-purifies with skeletal muscle **integrins** has resulted in an antibody directed against the avian **alpha-7 integrin** subunit. The specificity of the antibody was established by patterns of tissue staining and cross-reactivity with antibodies directed against the cytoplasmic domain of the rat **alpha-7** cytoplasmic domain. On sections of adult skeletal muscle the **alpha-7 integrin** was enriched in the myotendinous junction (MTJ). This localization was unique as neither the alpha-1, alpha-3, alpha-5, alpha-6 and alpha-v subunit localizes in the myotendinous junction. The distribution of the **alpha-7** subunit in the MTJ was examined during embryonic development. **alpha-7** expression in the junction is first apparent around embryo day 14 and is almost exclusively at the developing MTJ at this stage. alpha-3 is expressed with distinctive punctate staining around the junctional area in earlier embryos (11-day). The time of appearance of the **alpha-7** subunit in the MTJ correlates with the insertion of myofibrils into subsarcolemmal densities and folding of the junctional membrane, suggesting a role of the **alpha-7 integrin** in this process. Vinculin is present throughout development of the myotendinous junction, suggesting that the **alpha-7 integrin** recognizes a preformed cytoskeletal structure. The presence of the **alpha-7** subunit in the myotendinous junction and the alpha-5 subunit in the adhesion plaque demonstrates a molecular difference between these two adherens junctions. It also points to possible origins of junctional specificity on muscle. Differences between these two junctions were developed further using an antibody against phosphotyrosine (PY20). Phosphotyrosine is thought to participate in the organization and stabilization of adhesions. The focal adhesion and the neuromuscular junction, but not the MTJ, contained proteins phosphorylated on tyrosine.
CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10506
Muscle - Physiology and Biochemistry *17504
Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18014
Developmental Biology - Embryology - General and Descriptive *25502
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Muridae *86515
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Development; Membranes (Cell Biology); Muscular System (Movement and Support); Skeletal System (Movement and Support)
IT Chemicals & Biochemicals
INTEGRIN; PHOSPHOTYROSINE
IT Miscellaneous Descriptors
CYTOSKELETON; EMBRYONIC DEVELOPMENT; MUSCLE DEVELOPMENT; PHOSPHOTYROSINE
ORGN Super Taxa
Muridae; Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN 153-97-7 **INTEGRIN**
60781-49-6 **INTEGRIN**
21820-51-9 (PHOSPHOTYROSINE)

L22 ANSWER 22 OF 22 BIOSIS COPYRIGHT 1998 BIOLOGICAL ABSTRACTS INC.

AN 1992:324133 BIOSIS
DN BA94:29974
TI H36-**ALPHA-7** IS A NOVEL **INTEGRIN** ALPHA CHAIN THAT IS DEVELOPMENTALLY REGULATED DURING SKELETAL MYOGENESIS.
AU SONG W K; WANG W; FOSTER R F; BIELSER D A; **KAUFMAN S J**
CS DEP. CELL STRUCTURAL BIOL., UNIV. ILLINOIS, URBANA, ILL. 61801.
SO J CELL BIOL, (1992) 117 (3), 643-657.
CODEN: JCLBA3. ISSN: 0021-9525.
FS BA; OLD
LA English
AB H36 is a 120,000-D membrane glycoprotein that is expressed during the differentiation of skeletal muscle. H36 cDNA clones were isolated from a lambda UniZapXR rat myotube cDNA library and sequenced. The deduced amino acid sequence demonstrates that H36 is a novel **integrin** alpha chain that shares extensive homology with other alpha **integrins** that includes: (a) the GFFKR sequence found in all alpha **integrins**; (b) a single membrane spanning region; (c) conservation of 18 of 22 cysteines; and (d) a protease cleavage site found in the non-I region **integrin** alpha chains. The cytoplasmic domain of H36 is unique and additional regions of nonhomology further indicate H36 is distinct from all other alpha chains. In keeping with current nomenclature we designate this alpha chain **.alpha.7**. Northern blots demonstrate that expression of H36-**.alpha.7** mRNA is regulated both early in the development of the myogenic lineage and later, during terminal differentiation. Detection of H36-**.alpha.7** mRNA coincides with conversion of H36- myogenic precursor cells to H36+ cells. H36-**.alpha.7** mRNA is present in replicating myoblasts: expression increases upon terminal differentiation and is markedly reduced in developmentally defective myoblasts. In addition, H36-**.alpha.7** mRNA is not detected in C3H10T1/2 cells. It is in myotubes derived from myoblasts obtained by treatment of 10T1/2 cells with azacytidine or transfection with MRF4. Immunoblots and immunofluorescence demonstrate that the H36-**.alpha.7** chain is associated with **integrin .beta.1**. Affinity chromatography demonstrates that H36-**.alpha.7** **.beta.1** selectively binds to laminin. The expression of H36-**.alpha.7** on secondary myoblasts during the development of the limb in vivo corresponds with the appearance of laminin in the limb, with the responsiveness of secondary myoblast proliferation to laminin, and with the onset of increased muscle mass, suggesting that H36-**.alpha.7** modulates this stage in limb development. We conclude that H36-**.alpha.7** is a novel alpha **integrin** laminin binding protein whose expression is developmentally regulated during skeletal myogenesis.
CC Cytology and Cytochemistry - Animal *03506
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules *10506
Metabolism - Proteins, Peptides and Amino Acids *13012
Muscle - Physiology and Biochemistry *17504
Developmental Biology - Embryology - Morphogenesis, General *25514
BC Muridae 46375
IT Miscellaneous Descriptors
RAT LAMININ AMINO ACID SEQUENCE MOLECULAR SEQUENCE DATA
RN 133-37-7, 61791-43-3 **INTEGRIN**

=> fil medline
FILE 'MEDLINE' ENTERED AT 12:13:48 ON 19 MAY 2003

FILE LAST UPDATED: 9 MAY 2003 (20030509/UP). FILE COVERS 1951 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RELOAD for details.

MEDLINE thesauri in the CN, CT, and MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L83 ANSWER 1 OF 45 MEDLINE
AN 2003204286 IN-PROCESS
DN 2.610054 PubMed ID: 12670877
TI Constitutive properties, not molecular adaptations, mediate extraocular muscle sparing in dystrophic mdx mice.
AU Porter John D; Merriam Anita P; Khanna Sangeeta; Andrade Francisco H; Richmonds Chelliah R; Leahy Patrick; Cheng Georgiana; Karathanasis Paraskevi; Zhou Xiaohua; Kusner Linda L; Adams Marvin E; Willem Michael; Mayer Ulrike; Kaminski Henry J
CS Department of Ophthalmology, Case Western Reserve University and The Research Institute of University Hospitals of Cleveland, 11100 Euclid Ave., Cleveland, Ohio 44106-5068, USA.. jdp7@po.cwru.edu
SO FASEB JOURNAL, (2003 May) 17 (8) 893-5.
Journal code: 8804484. ISSN: 1530-6860.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030502
Last Updated in STN: 20030502
AB Extraocular muscle (EOM) is spared in Duchenne **muscular dystrophy**. Here, we tested putative EOM sparing mechanisms predicted from existing dystrophinopathy models. Data show that mdx mouse EOM contains dystrophin-glycoprotein complex (DGC)-competent and DGC-deficient myofibers distributed in a fiber type-specific pattern. Up-regulation of a dystrophin homologue, utrophin, mediates selective DGC retention. Counter to the DGC mechanical hypothesis, an intact DGC is not a precondition for EOM sarcolemmal integrity, and active adaptation at the level of calcium homeostasis is not mechanistic in protection. A partial, fiber type-specific retention of antiischemic nitric oxide to vascular smooth muscle signaling is not a factor in EOM sparing, because mice deficient in dystrophin and alpha-syntrophin, which localizes neuronal nitric oxide synthase to the sarcolemma, have normal EOMs. Moreover, an alternative transmembrane protein, **alpha7beta1 integrin**, does not appear to substitute for the DGC in EOM. Finally, genomewide expression profiling showed that EOM does not actively adapt to dystrophinopathy but identified candidate genes for the constitutive protection of mdx EOM. Taken together, data emphasize the conditional nature of dystrophinopathy and the potential importance of nonmechanical DGC roles and support the hypothesis that broad, constitutive structural cell signaling, and/or biochemical differences between EOM and other skeletal muscles are determinants of differential disease responsiveness.

L83 ANSWER 2 OF 45 MEDLINE
AN 2003174192 IN-PROCESS
DN 22579828 PubMed ID: 12691739
TI Involvement of **alpha7beta1 integrin** in the conditioning-lesion effect on sensory axon regeneration.
AU Ekstrom Per A R; Mayer Ulrike; Ranjwani Alisa; Pountney David; Birney John; Tonge David A
CS Department of Animal Physiology, University of Lund, Helgonavagen 3B, SE-223 62, Lund, Sweden..

SO MOLECULAR AND CELLULAR NEUROSCIENCES, 2003 Mar 22 3 343-55.
Journal code: 9105088. ISSN: 1044-7431.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030416
Last Updated on STN: 20030416
AB Conditioning lesions of peripheral nerves improve axonal regeneration after injury and involve changes in expression of proteins required for axonal growth. **Integrin alpha7beta1** expression in motor and sensory neurons increases following nerve lesions and motor axon regeneration is impaired in **alpha7 integrin** KO mice (J. Neurosci. 20, 1822-1830). To investigate the role of **alpha7beta1 integrin** in sensory axon regeneration, dorsal root ganglia of adult mice were cultured in gels of laminin-rich extracellular matrix (Matrigel) or collagen. Normal dorsal root ganglia in Matrigel or collagen supplemented with laminin showed spontaneous axonal outgrowth, which was greatly increased in conditioned preparations, but only in the presence of laminin. Conditioned dorsal root ganglia from normal mice cultured with a blocking antibody to **beta1 integrin** and from **alpha7 integrin** KO mice showed reduced axonal growth in both Matrigel- and laminin-supplemented collagen gels. Enhanced axonal regeneration after conditioning lesions therefore involves increased responsiveness to laminin and **integrin alpha7beta1** expression.

L83 ANSWER 3 OF 45 MEDLINE
AN **2003116386** IN-PROCESS
DN **22476683** PubMed ID: **12588796**
TI Defective **integrin** switch and matrix composition at **alpha** 7-deficient myotendinous junctions precede the onset of **muscular dystrophy** in mice.
AU Nawrotzki Ralph; Willem Michael; Miosge Nicolai; Brinkmeier Heinrich; Mayer Ulrike
CS Max-Planck-Institute for Biochemistry, 82152 Martinsried, Germany.
SO HUMAN MOLECULAR GENETICS, (2003 Mar 1) 12 (5) 483-95.
Journal code: 9208958. ISSN: 0964-6906.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030313
Last Updated on STN: 20030313
AB Force transmission at the myotendinous junction requires a strong link between the muscle cytoskeleton and the extracellular matrix. At the adult junction, two splice variants of the laminin-binding **integrins**, **alpha7Abeta1D** and **alpha7Bbeta1D**, are highly enriched. The **alpha7** subunits are critical for the integrity of the junctional sarcolemma because **integrin alpha7**-deficient mice develop **muscular dystrophy**, primarily affecting this site of the muscle. Here, we report that beta1D **integrin** coimmunoprecipitates and colocalizes with the alpha1 subunit at **alpha7**-deficient junctions, but does not associate with alpha1, alpha7 or alpha7 **integrins**. By immunogold labelling we show that the basement membranes of **integrin alpha7**-deficient muscles recruit abnormally high levels of fibronectin, the ligand of alpha5beta1. Finally, we demonstrate that alpha5beta1 is down-regulated at the normal postnatal junction and is displaced by **alpha7beta1D**. These results suggest that the **alpha7** subunit is implicated in the down-regulation of alpha5beta1 and in the removal of fibronectin from the maturing myotendinous junction, thus providing an **alpha7beta1D**

-based link to laminin. We propose that the persistence of alpha6beta1 in **alpha7**-deficient mice is not compatible with normal muscle function and leads to muscle wasting.

L53 ANSWER 4 OF 45 MEDLINE

AN 2003115827 MEDLINE
DN 22516254 PubMed ID: 12629182
TI Sensory neuron subtypes have unique substratum preference and receptor expression before target innervation.
AU Guan Wei; Puthenveedu Manojkumar A; Condic Maureen L
CS Department of Neurobiology and Anatomy, University of Utah, School of Medicine, Salt Lake City, Utah 84132-3401, USA.
NC R01 NS38138 (NINDS)
SO JOURNAL OF NEUROSCIENCE, (2003 Mar 1) 23 (5) 1781-91.
Journal code: 8102140. ISSN: 1529-2401.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20030312
Last Updated on STN: 20030325
Entered Medline: 20030324
AB The factors controlling the specification and subsequent differentiation of sensory neurons are poorly understood. Data from embryological manipulations suggest that either sensory neuron fates are specified by the targets they encounter or sensory neurons are considerably more "plastic" with respect to specification than are neurons of the CNS. The prevailing view that sensory neurons are specified late in development is not consistent, however, with the directed outgrowth of sensory neurons to their targets and the characteristic spatial distribution of sensory neuron fates within the peripheral ganglia. To address when in development different classes of sensory neurons can first be distinguished, we investigated the interactions of early dorsal root ganglia neurons with the extracellular matrix before neurite outgrowth to targets. We found that subclasses of sensory neurons in early dorsal root ganglia show different patterns of neurite outgrowth and **integrin** expression that are predictive of their fates. In the absence of neurotrophins, presumptive proprioceptive neurons extend neurites robustly on both laminin and fibronectin, whereas presumptive cutaneous neurons show a strong preference for laminin. Cutaneous afferents that have innervated targets show a similar strong preference for laminin and show higher levels of **integrin alpha7beta1** than do proprioceptive neurons. Finally, presumptive proprioceptive neurons express fibronectin receptors, **integrin** alpha3beta1, alpha4beta1, and alpha5beta1, at higher levels than do presumptive cutaneous neurons. Our results indicate that subtypes of sensory neurons have unique patterns of neurite outgrowth and receptor expression before target innervation.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Cell Differentiation: DE, drug effects
Cell Differentiation: PH, physiology
Chick Embryo
Extracellular Matrix: ME, metabolism
Fibronectins: ME, metabolism
Fibronectins: PD, pharmacology
*Ganglia, Spinal: CY, cytology
*Ganglia, Spinal: EM, embryology
Ganglia, Spinal: ME, metabolism
Integrins: BI, biosynthesis
Integrins: GE, genetics
Laminin: ME, metabolism
Laminin: PD, pharmacology

Nerve Growth Factor: PD, pharmacology
Neurites: DE, drug effects
Neurites: PH, physiology
*Neurons, Afferent: CL, classification
*Neurons, Afferent: CY, cytology
Neurons, Afferent: DE, drug effects
Neurons, Afferent: ME, metabolism
Neurotrophin 3: PD, pharmacology
RNA, Messenger: BI, biosynthesis
Receptor, trkA: BI, biosynthesis
Receptor, trkC: BI, biosynthesis
*Receptors, Cell Surface: BI, biosynthesis
Receptors, Fibronectin: BI, biosynthesis
RN 9061-61-4 (Nerve Growth Factor)
CN 0 (Fibronectins); 0 (**Integrins**); 0 (Laminin); 0 (Neurotrophin 3); 0 (RNA, Messenger); 0 (Receptors, Cell Surface); 0 (Receptors, Fibronectin); EC 2.7.1.112 (Receptor, trkA); EC 2.7.1.112 (Receptor, trkC)

L83 ANSWER 5 OF 45 MEDLINE
AN 2002454819 MEDLINE
DN 22201697 PubMed ID: 12213731
TI Expression of **alpha7beta1 integrin** splicing variants during skeletal muscle regeneration.
AU Kaariainen Minna; Nissinen Liisa; Kaufman Stephen; Sonnenberg Arnoud; Jarvinen Markku; Heino Jyrki; Kalimo Hannu
CS Medical School and the Institute of Medical Technology, University of Tampere, Finland.
SO AMERICAN JOURNAL OF PATHOLOGY, (2002 Sep) 161 (3) 1023-31.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200209
ED Entered STN: 20020906
Last Updated on STN: 20020928
Entered Medline: 20020927
AB **Integrin alpha7beta1** is a laminin receptor, both subunits of which have alternatively spliced, developmentally regulated variants. In skeletal muscle **beta1** has two major splice variants of the intracellular domain (beta1A and beta1D). **alpha7X1** and **alpha7X2** represent variants of the **alpha7** ectodomain, whereas **alpha7A** and **alpha7B** are variants of the intracellular domain. Previously we showed that during early regeneration after transection injury of muscle **alpha7** **integrin** mediates dynamic adhesion of myofibers along their lateral aspects to the extracellular matrix. Stable attachment of myofibers to the extracellular matrix occurs during the third week after injury, when new myotendinous junctions develop at the ends of the regenerating myofibers. Now we have analyzed the relative expression of beta1A/beta1D and **alpha7A**/**alpha7B** and **alpha7X1**/**alpha7X2** isoforms during regeneration for 2 to 56 days after transection of rat soleus muscle using reverse **transcriptase**-polymerase chain reaction and immunohistochemistry. During early regeneration beta1A was the predominant isoform in both the muscle and scar tissue. Expression of muscle-specific beta1D was detected in regenerating myofibers from day 4 onwards, ie, when myogenic mitotic activity began to decrease, and it became more abundant with the progression of regeneration. **alpha7B** isoform predominated on day 2. Thereafter, the relative expression of **alpha7A** **transcripts** increased until day 7 with the concomitant appearance of **alpha7A** immunoreactivity on regenerating myofibers. Finally, **alpha7B** again became the predominant variant in highly regenerated

myofibers. Similarly as in the controls, **alpha7X1** and **alpha7X2** isoforms were both expressed throughout the regeneration with a peak in **alpha7X1** expression on day 4 coinciding with the dynamic adhesion stage. The results suggest that during regeneration of skeletal muscle the splicing of **beta1** and **alpha7** **integrin** subunits is regulated according to functional requirements. **alpha7A** and **alpha7X1** appear to have a specific role during the dynamic phase of adhesion, whereas **alpha7B**, **alpha7X2**, and beta1D predominate during stable adhesion.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
*Integrins: BI, biosynthesis
*Integrins: GE, genetics
Muscle, Skeletal: ME, metabolism
*Muscle, Skeletal: PH, physiology
Protein Structure, Tertiary: GE, genetics
RNA Splicing
Rats
Rats, Sprague-Dawley
*Regeneration: PH, physiology

CN 0 (**Integrins**); 0 (**integrin alpha7beta1**)

L83 ANSWER 6 OF 45 MEDLINE
AN 21002315192 MEDLINE
DN 21052264 PubMed ID: 12057917
TI **Integrin alpha 7 beta 1** in **muscular dystrophy**/myopathy of unknown etiology.
AU Pegoraro Elena; Depellare Fulvio; Prandini Paola; Marin Alessandra; Fanin Marina; Trevisan Carlo P; El-Messlemani Abdul Hassib; Tarone Guido; Engvall Eva; Hoffman Eric P; Angelini Corrado
CS Neuromuscular Center, Department of Neurological and Psychiatric Sciences, University of Padova, Padova, Italy.. elena.pegoraro@unipd.it
SO AMERICAN JOURNAL OF PATHOLOGY, (2002 Jun) 160 (6) 2135-43.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200207
ED Entered STN: 20020611
Last Updated on STN: 20020809
Entered Medline: 20010718
AB To investigate the role of **integrin alpha 7** in muscle pathology, we used a "candidate gene" approach in a large cohort of **muscular dystrophy**/myopathy patients. Antibodies against the intracellular domain of the **integrin alpha** **7A** and **alpha 7B** were used to stain muscle **biopsies** from 210 patients with **muscular** **dystrophy**/myopathy of unknown etiology. Levels of **alpha** **7A** and **alpha 7B** **integrin** were found to be decreased in 35 of 210 patients (approximately 17%). In six of these patients no **integrin alpha 7B** was detected. **Screening** for **alpha 7B** mutation in 30 of 35 patients detected only one **integrin alpha** **7** missense mutation (the mutation on the second allele was not found) in a patient presenting with a congenital **muscular** **dystrophy**-like phenotype. No **integrin alpha** **7** gene mutations were identified in all of the other patients showing **integrin alpha 7** deficiency. In the process of mutation analysis, we identified a novel **integrin** **alpha 7** isoform presenting 72-bp deletion. This isoform results from a partial deletion of exon 21 due to the use of a cryptic splice site generated by a G to A missense mutation at nucleotide position

2644 in **integrin alpha 7** cDNA. This spliced isoform is present in about 12% of the chromosomes studied. We conclude that secondary **integrin alpha 7** deficiency is rather common in **muscular dystrophy** myopathy of unknown etiology, emphasizing the multiple mechanisms that may modulate **integrin** function and stability.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Alternative Splicing
Biopsy
Child
Child, Preschool
Down-Regulation
Fluorescent Antibody Technique
Infant
Integrins: DF, deficiency
Integrins: GE, genetics
***Integrins: PH, physiology**
Muscles: PA, pathology
Muscular Diseases: PA, pathology
*Muscular Diseases: PP, physiopathology
Muscular Dystrophies: PA, pathology
***Muscular Dystrophies: PP, physiopathology**
Mutation
Mutation, Missense
Oligonucleotide Array Sequence Analysis
Polymorphism, Single-Stranded Conformational
RNA, Messenger: ME, metabolism
Restriction Mapping
Reverse Transcriptase Polymerase Chain Reaction

CN 0 (**Integrins**); 0 (RNA, Messenger); 0 (**integrin alpha7beta1**)

L83 ANSWER 7 OF 45 MEDLINE
AN 2002210291 MEDLINE
DN 21881641 PubMed ID: 11884516
TI Association of the tetraspanin CD151 with the laminin-binding **integrins** alpha3beta1, alpha6beta1, alpha6beta4 and **alpha7beta1** in cells in culture and in vivo.
CM Erratum in: J Cell Sci 2002 Jun 15;115(Pt 12):2615
AU Sterk Lotus M T; Geuijen Cecile A W; van den Berg Jose G; Claessen Nike; Weening Jan J; Sonnenberg Arnoud
CS Division of Cell Biology, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.
SO JOURNAL OF CELL SCIENCE, (2002 Mar 15) 115 (Pt 6) 1161-73.
Journal code: 0052457. ISSN: 0021-9533.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200210
ED Entered STN: 20020412
Last Updated on STN: 20021217
Entered Medline: 20021008
AB CD151 is a cell surface protein that belongs to the tetraspanin superfamily. It forms complexes with the laminin-binding **integrins** alpha3beta1, alpha6beta1 and alpha6beta4 and is redistributed with these **integrins** in many tissues at sites of cell-matrix interactions. In this study we show that CD151 can also form stable complexes with the laminin-binding **integrin alpha7beta1**. The strength of this interaction is comparable to that between CD151 and alpha3beta1. Complexes of alpha3beta1, alpha6beta1 and **alpha7beta1** with CD151 are equally well formed with all splice variants of the alpha3, alpha6 and **alpha7** subunits, and

complex formation is not affected by mutations that prevent the cleavage of the **integrin** alpha6 subunit. Like the expression of alpha3beta1 and alpha6beta1, expression of **alpha7beta1** in K562 cells results in increased levels of CD151 at its surface. Two non-**integrin** laminin receptors, dystroglycan and the polypeptide on which the Lutheran blood group antigens are expressed, are also often colocalized with CD151, but no association with CD151-alpha3beta1 complexes was found with biochemical analysis. The anti-CD151 antibody TS151R detects an epitope at a site at which CD151 interacts with **integrins**, and therefore it cannot react with CD151 when it is bound to an **integrin**. Comparison of the staining patterns produced by TS151R with that by of an anti-CD151 antibody recognizing an epitope outside the binding site (P48) revealed that most tissues expressing one or more laminin-binding **integrins** reacted with P48 but not with TS151R. However, smooth muscle cells that express **alpha7beta1** and renal tubular epithelial cells that express alpha6beta1 were stained equally well by TS151R and P48. These results suggest that the interactions between CD151 and laminin-binding **integrins** are subject to cell-type-specific regulation.

CT Check Tags: Human; Support, Non-U.S. Gov't
Antibodies, Monoclonal: IM, immunology
Antigens, CD: IM, immunology
*Antigens, CD: ME, metabolism
*Antigens, Surface: ME, metabolism
Cells, Cultured
Cytoskeletal Proteins: PH, physiology
Epitopes: IM, immunology
Integrin alpha3beta1
Integrin alpha6beta1
Integrin alpha6beta4
***Integrins: ME, metabolism**
K562 Cells
Kidney Glomerulus: ME, metabolism
Kidney Glomerulus: UL, ultrastructure
Kidney Tubules: CY, cytology
Kidney Tubules: ME, metabolism
Kidney Tubules: UL, ultrastructure
Lutheran Blood-Group System: PH, physiology
Membrane Glycoproteins: PH, physiology
Muscles: AH, anatomy & histology
Muscles: CY, cytology
Muscles: ME, metabolism
Muscles: UL, ultrastructure
Receptors, Laminin: ME, metabolism
Skin: CY, cytology
Skin: ME, metabolism
Skin: UL, ultrastructure

RN 146888-27-9 (43-156K dystrophin-associated glycoprotein)

CN 0 (Antibodies, Monoclonal); 0 (Antigens, CD); 0 (Antigens, Surface); 0 (CD151 antigen, human); 0 (Cytoskeletal Proteins); 0 (Epitopes); 0 (**Integrin** alpha3beta1); 0 (**Integrin** alpha6beta1); 0 (**Integrin** alpha6beta4); 0 (**Integrins**); 0 (Lutheran Blood-Group System); 0 (Membrane Glycoproteins); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

L49 ANSWER 6 OF 45 MEDLINE
AN 21[illegible] MEDLINE
DN 21439089 PubMed ID: 11744718
TI Alternative splice variants of **alpha 7 beta 1 integrin** selectively recognize different laminin isoforms.
AU Van der Mark Helga; Williams Inka; Wendler Olaf; Strickin Lydia; von der Mark Klaus; Bosch Ernst

CS Friedrich-Alexander-Universitat Erlangen-Nurnberg, Nikolaus-Fiebiger-Zentrum fur Molekulare Medizin, Department of Experimental Medicine I, 91054 Erlangen, Germany.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, 2002 Feb 22 277 (8) 6010-6.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020227
Last Updated on STN: 20030109
Entered Medline: 20020424
AB The **integrin alpha(7)beta(1)** occurs in several cytoplasmic (**alpha(7A)**, **alpha(7B)**) and extracellular splice variants (alpha(7X1), alpha(7X2)), which are differentially expressed during development of skeletal and heart muscle. The extracellular variants result from the alternative splicing of exons X1 and X2, corresponding to a segment within the putative ligand binding domain. To study the specificity and affinity of the X1/X2 variants to different laminin isoforms, soluble **alpha(7)beta(1)** complexes were prepared by recombinant coexpression of the extracellular domains of the alpha- and beta-subunits. The binding of these complexes to purified ligands was measured by solid phase binding assays. Surprisingly, the alternative splice variants revealed different and specific affinities to different laminin isoforms. While the alpha(7X2) variant bound much more strongly to laminin-1 than the alpha(7X1) variant, the latter showed a high affinity binding to laminins-8 and -10/11. Laminin-2, the major laminin isoform in skeletal muscle, was recognized by both variants, whereas none of the two variants were able to interact with laminin-5. A specific blocking antibody inhibited the binding of both variants to all laminins tested, indicating the involvement of common epitopes in alpha(7X1)**beta(1)** and alpha(7X2)**beta(1)**. Because laminin-8 and -10/11 as well as alpha(7X1) are expressed in developing skeletal and cardiac muscle, these findings suggest that alpha(7X1)**beta(1)** may represent a physiological receptor with novel specificities for laminin-8 and -10.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Alternative Splicing
Binding Sites
Dimerization
*Integrins: GE, genetics
*Integrins: ME, metabolism
Kinetics
*Laminin: ME, metabolism
Mice
Myocardium: ME, metabolism
Protein Isoforms: ME, metabolism
Protein Subunits
Recombinant Proteins: ME, metabolism
Tumor Cells, Cultured
*Variation (Genetics)
CN 1 **Integrins** ; 1 Laminin ; 1 Protein Isoforms ; 1 Protein Subunits ; 1 Recombinant Proteins ; 1 **integrin alpha7beta1** ; 1 laminin 1

L14 ANSWER 9 OF 48 MEDLINE
AN 2001641852 MEDLINE
DN 21851142 PubMed ID: 11694741
TI The role of **integrins** in human embryo implantation.
AU Merviel P; Challier J C; Carbillon L; Foidart J M; Uzan S
CS Service de Gynecologie-Obstetrique et Medecine de la Reproduction, Hopital

Tenon, Paris, France.. philippe.merviel@tnn.ap-hop-paris.fr
SO FETAL DIAGNOSIS AND THERAPY, (2001 Nov-Dec) 16 (6) 364-71. Ref: 42
Journal code: 9107483. ISSN: 1015-3837.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200201
ED Entered STN: 20011107
Last Updated on STN: 20020125
Entered Medline: 20020116
AB **Integrins** are adhesion molecules present in endometrial, decidual, and extravillous cytotrophoblast (EVCT) cells. They participate in cell-cell adhesion as well as in adhesion between cells and components of the extracellular matrix, and they play an important role in the endometrial phenotype change that occurs during the secretory phase, the first stage of implantation. At the beginning of pregnancy, the change in **integrin** expression is synchronized with the trophoblast attachment (embryo-endometrium interactions with **integrins** alpha(v)beta3, alpha4beta1, alpha6beta1, and **alpha7beta1**) and the embryo's invasion of the decidua (**integrins** alpha6beta4-->alpha5beta1-->alpha1beta1-->alpha4beta1 switch from proliferative to endovascular EVCT). Several diseases, including preeclampsia, intrauterine growth retardation caused by vascular problems and defective luteal phases, may be explained by anomalies in **integrin** patterns.
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CT Check Tags: Female; Human
Cell Adhesion Molecules: PH, physiology
*Embryo Implantation: PH, physiology
Endometriosis
Infertility, Female
***Integrins: PH, physiology**
Pre-Eclampsia
Pregnancy
Trophoblasts: CY, cytology
Trophoblasts: PH, physiology
CN 0 (Cell Adhesion Molecules); 0 (**Integrins**)

L83 ANSWER 10 OF 45 MEDLINE
AN 2001515891 MEDLINE
DN 21234604 PubMed ID: 11329371
TI HEMCAM/CD146 downregulates cell surface expression of **beta1 integrins**.
AU Alais S; Allioli N; Pujades C; Duband J L; Vainio O; Imhof B A; Dunon D
CS UMR-CNRS 7622, Universite Pierre et Marie Curie, Paris, France.
SO JOURNAL OF CELL SCIENCE, (2001 May) 114 (Pt 10) 1847-56.
Journal code: 0052457. ISSN: 0021-9533.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010824
Last Updated on STN: 20010824
Entered Medline: 20010621
AB HEMCAM/gicerin, an immunoglobulin superfamily protein, is involved in homophilic and heterophilic adhesion. It interacts with NGF neurite outgrowth factor , a molecule of the laminin family. Alternative splicing leads to mRNAs coding for HEMCAM with a short HEMCAM-s or a long cytoplasmic tail HEMCAM-l . To investigate the cellular function of

these two variants, we stably transfected murine fibroblasts with either form of HEMCAM. Expression of each isoform of this protein in L cells delayed proliferation and modified their adhesion properties to purified extracellular matrix proteins. Expression of either HEMCAM-s or HEMCAM-l inhibited **integrin**-dependent adhesion and spreading of fibroblasts to laminin 1, showing that this phenomenon did not depend on the cytoplasmic region. By contrast, L-cell adhesion and spreading to fibronectin depended on the HEMCAM isoform expressed. Flow cytometry and immunoprecipitation studies revealed that the expression of HEMCAM downregulated expression of the laminin-binding **integrins** alpha3beta1, alpha6beta1 and **alpha7beta1**, and fibronectin receptor alpha5beta1 from the cell surface. Semi-quantitative PCR and northern blot experiments showed that the expression of alpha6beta1 **integrin** modified by HEMCAM occurred at a **translation** or maturation level. Thus, our data demonstrate that HEMCAM regulates fibroblast adhesion by controlling **beta1 integrin** expression.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Antigens, CD29: GE, genetics
*Antigens, CD29: ME, metabolism
Antigens, Surface: GE, genetics
Antigens, Surface: ME, metabolism
Cell Adhesion: PH, physiology
*Cell Adhesion Molecules: GE, genetics
*Cell Adhesion Molecules: ME, metabolism
Cell Division: PH, physiology
Cell Movement: PH, physiology
Cells, Cultured
Chick Embryo
Down-Regulation: PH, physiology
Fibroblasts: CY, cytology
Fibroblasts: ME, metabolism
Flow Cytometry
Gene Expression Regulation, Developmental
Integrin alpha6beta1
Integrins: GE, genetics
Integrins: ME, metabolism
Membrane Proteins: GE, genetics
Membrane Proteins: ME, metabolism
Mice
Molecular Sequence Data
RNA, Messenger: AN, analysis
Sequence Homology, Amino Acid
Transcription, Genetic: PH, physiology
Transfection

CN 0 (Antigens, CD29); 0 (Antigens, Surface); 0 (Cell Adhesion Molecules); 0 (HEMCAM protein); 0 (**Integrin** alpha6beta1); 0 (**Integrins**); 0 (MCAM protein, human); 0 (Membrane Proteins); 0 (RNA, Messenger)

L83 ANSWER 11 OF 45 MEDLINE
AN 2001268248 MEDLINE
DN 21258472 PubMed ID: 11361006
TI Transfection of MCF-7 carcinoma cells with human **integrin alpha7** cDNA promotes adhesion to laminin.
AU Vizirianakis I S; Yao C C; Chen Y; Ziober B L; Tsiftsoglou A S; Kramer R H
CS Department of Stomatology, University of California at San Francisco, 94143-0512, USA.
SO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (2001 Jan 1) 385 (1) 108-16.
Journal code: 0372430. ISSN: 0003-9861.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

DN GENBANK-AF072132
EM 200106
ED Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621
AB The laminin-binding **alpha7beta1 integrin** receptor is highly expressed by skeletal and cardiac muscles, and has been suggested to be a crucial molecule during myogenic cell migration and differentiation. Absence of **integrin alpha7** subunit contributes to a form of **muscular dystrophy** in **integrin alpha7** null mice, whereas specific mutations in the **alpha7** gene are associated in humans with congenital myopathy. To examine in more detail the potential role of **integrin alpha7** in human-related muscular disorders, we cloned **alpha7** cDNA by RT-PCR from human skeletal muscle mRNA and then expressed the full-length human **integrin alpha7** cDNA by transfection in several cell lines including MCF-7, COS-7, and NIH3T3 cells. The isolated cDNA corresponds to the human **alpha7X2B** alternative splice form. Expression of human **alpha7** was further confirmed by transfection of chimeric human/mouse **alpha7** cDNA constructs. To demonstrate the functionality of expressed human **alpha7**, adhesion experiments with transfected MCF-7 cells have confirmed the specific binding of human **alpha7** to laminin. In addition, mouse polyclonal and monoclonal antibodies were generated against the extracellular domain of human **alpha7** and used to analyze by flow cytometry MCF-7 and NIH3T3 cells transfected with the full-length of human **alpha7** cDNA. These results show for the first time the exogenous expression of functional full-length human **alpha7** cDNA, as well as the development of monoclonal antibodies against the human **alpha7** extracellular domain. Antibodies developed will be useful for further analysis of human disorders involving **alpha7** dysfunction and facilitate isolation of muscle stem cells (satellite cells) and thereby expand the opportunities for genetically modified transplantation treatment of human disease.
CT Check Tags: Animal; Human
3T3 Cells
Alternative Splicing
Antibodies, Monoclonal: ME, metabolism
*Antigens, CD: GE, genetics
Antigens, CD: ME, metabolism
Biotin: ME, metabolism
Blotting, Western
*Breast Neoplasms: ME, metabolism
*Breast Neoplasms: PA, pathology
COS Cells
Cell Adhesion
Cell Line
Cell Separation
Cloning, Molecular
DNA, Complementary: ME, metabolism
Flow Cytometry
Immunohistochemistry
*Laminin: ME, metabolism
Mice
Molecular Sequence Data
Muscle, Skeletal: ME, metabolism
Precipitin Tests
Protein Structure, Tertiary
RNA, Messenger: ME, metabolism
Reverse Transcriptase Polymerase Chain Reaction
Transfection
Tumor Cells, Cultured

RN 58-85-5 Biotin
CN 9 Antibodies, Monoclonal ; 1 Antigens, CD ; 1 DNA, Complementary ; 1 "ITGA7" protein, human ; 1 Laminin ; 1 RNA, Messenger ; 1 laminin 1

L63 ANSWER 12 OF 45 MEDLINE
AN 2001253114 MEDLINE
DN 21220787 PubMed ID: 11319864
TI Laminin-induced change in conformation of preexisting **alpha7beta1 integrin** signals secondary myofiber formation.
AU Blanco-Bose W E; Blau H M
CS Department of Molecular Pharmacology, Stanford University School of Medicine, Stanford, California 94305-5175, USA.
NC AR09521 (NIA)
CA59717 (NCI)
HD18179 (NICHD)
SO DEVELOPMENTAL BIOLOGY, (2001 May 1) 233 (1) 148-60.
Journal code: 0372762. ISSN: 0012-1606.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010604
Last Updated on STN: 20010604
Entered Medline: 20010531
AB Two distinct populations of myoblasts, distinguishable by **alpha7 integrin** expression have been hypothesized to give rise to two phases of myofiber formation in embryonic limb development. We show here that **alpha7 integrin** is detectable far earlier than previously reported on both "primary" and "secondary" lineage myoblasts and myofibers. An antibody (1211) that recognizes an intracellular epitope allowed detection of **alpha7 integrin** previously missed using an antibody (H36) that recognizes an extracellular epitope. We found that when myoblasts were isolated and cultured from different developmental stages, H36 only detected **alpha7 integrin** that was in direct contact with its ligand, laminin. Moreover, **alpha7 integrin** detection by H36 was reversible and highly localized to subcellular points of contact between myoblasts and laminin-coated 2.8-microm microspheres. Prior to secondary myofiber formation in limb embryogenesis, laminin was present but not in close proximity to clusters of primary myofibers that expressed **alpha7 integrin** detected by antibody 1211 using deconvolution microscopy. These results suggest that the timing of the interaction of preexisting **alpha7 integrin** with its ligand, laminin, is a major determinant of allosteric changes that result in an activated form of **alpha7 integrin** capable of transducing signals from the extracellular matrix commensurate with secondary myofiber formation.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Animals, Newborn
Antibody Specificity
Antigens, CD: GE, genetics
Antigens, CD: IM, immunology
Cell Compartmentation
Cell Differentiation
Cells, Cultured
Collagen: ME, metabolism
Hindlimb: CY, cytology
Integrins: CH, chemistry
***Integrins: ME, metabolism**
*Laminin: ME, metabolism
*Muscle Fibers: CY, cytology

*Muscle, Skeletal: CY, cytology
Protein Conformation
RNA, Messenger
Rats
Rats, Sprague-Dawley
Receptors, Laminin: CH, chemistry
*Receptors, Laminin: ME, metabolism
Signal Transduction
*Stem Cells: CY, cytology
Tissue Culture
RN 9007-34-5 (Collagen)
CN 0 (Antigens, CD); 0 (ITGA7 protein, human); 0 (**Integrins**); 0 (Laminin); 0 (RNA, Messenger); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

L83 ANSWER 13 OF 45 MEDLINE
AN 2001227981 MEDLINE
DN 21157400 PubMed ID: 11257121
TI Enhanced expression of the **alpha 7 beta 1 integrin** reduces **muscular dystrophy** and restores viability in dystrophic mice.
AU Burkin D J; Wallace G Q; Nicol K J; Kaufman D J; Kaufman S J
CS Department of Cell and Structural Biology, University of Illinois, Urbana, Illinois 61801, USA.
SO JOURNAL OF CELL BIOLOGY, (2001 Mar 19) 152 (6) 1207-18.
Journal code: 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010503
Last Updated on STN: 20010502
Entered Medline: 20010426
AB Muscle fibers attach to laminin in the basal lamina using two distinct mechanisms: the dystropnin glycoprotein complex and the **alpha 7 beta 1 integrin**. Defects in these linkage systems result in Duchenne **muscular dystrophy** (DMD), alpha 2 laminin congenital **muscular dystrophy**, sarcoglycan-related **muscular dystrophy**, and **alpha 7 integrin** congenital **muscular dystrophy**. Therefore, the molecular continuity between the extracellular matrix and cell cytoskeleton is essential for the structural and functional integrity of skeletal muscle. To test whether the **alpha 7 beta 1 integrin** can compensate for the absence of dystrophin, we expressed the rat **alpha 7** chain in mdx/utr(-/-) mice that lack both dystrophin and utrophin. These mice develop a severe **muscular dystrophy** highly akin to that in DMD, and they also die prematurely. Using the muscle creatine kinase promoter, expression of the alpha 7BX2 **integrin** chain was increased 2.0-2.3-fold in mdx/utr(-/-) mice. Concomitant with the increase in the **alpha 7** chain, its heterodimeric partner, beta 1D, was also increased in the transgenic animals. Transgenic expression of the alpha 7BX2 chain in the mdx/utr(-/-) mice extended their longevity by threefold, reduced kyphosis and the development of muscle disease, and maintained mobility and the structure of the neuromuscular junction. Thus, bilateral **alpha 7 beta 1 integrin**-mediated association of muscle cells with the extracellular matrix alleviates many of the symptoms of disease observed in mdx utr - - mice and compensates for the absence of the dystrophin- and utrophin-mediated linkage systems. This suggests that enhanced expression of the **alpha 7 beta 1 integrin**

may provide a novel approach to treat DMD and other muscle diseases that arise due to defects in the dystrophin glycoprotein complex. A video that contrasts kyphosis, gait, joint contractures, and mobility in mdx utr - - and alpha TEM2-mdx utr -/- mice can be accessed at http://www.jcb.org/cgi/content/full/152/6/1201.

CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Blotting, Western
Body Weight
Contracture: PP, physiopathology
Creatine Kinase: GE, genetics
Cytoskeletal Proteins: GE, genetics
Cytoskeletal Proteins: ME, metabolism
Dystrophin: GE, genetics
Dystrophin: ME, metabolism
Hindlimb
Integrins: GE, genetics
***Integrins: ME, metabolism**
Isoenzymes: GE, genetics
Joints
Kyphosis
Magnetic Resonance Imaging
Membrane Proteins: GE, genetics
Membrane Proteins: ME, metabolism
Mice
Mice, Inbred mdx
Mice, Transgenic
Microscopy, Fluorescence
Muscle, Skeletal: PA, pathology
*Muscle, Skeletal: PP, physiopathology
Muscular Dystrophy, Animal: GE, genetics
Muscular Dystrophy, Animal: PA, pathology
Muscular Dystrophy, Animal: PP, physiopathology
Muscular Dystrophy, Duchenne: GE, genetics
Muscular Dystrophy, Duchenne: PA, pathology
***Muscular Dystrophy, Duchenne: PP, physiopathology**
Neuromuscular Junction: UL, ultrastructure
*Promoter Regions (Genetics)
Rats
Receptors, Cholinergic: ME, metabolism
Receptors, Cholinergic: UL, ultrastructure
Survival Rate
Transgenes

CN 0 (Cytoskeletal Proteins); 0 (Dystrophin); 0 (**Integrins**); 0 (Isoenzymes); 0 (Membrane Proteins,); 0 (Receptors, Cholinergic); 0 (dystrophin-related protein); 0 (**integrin alpha7beta1**); EC 2.7.3.2 (Creatine Kinase); EC 2.7.3.2.- (creatine kinase, MM form)

L83 ANSWER 14 OF 45 MEDLINE
AN 20310099994 MEDLINE
DN 20396592 PubMed ID: 10986444
TI Cell-cell adhesion via the ECM: **integrin** genetics in fly and worm.
AU Brown N H
CS Wellcome/CRC Institute and Department of Anatomy, University of Cambridge, Tennis Court Rd, CB2 1QP, Cambridge, UK.. nhb1@mole.bio.cam.ac.uk
SO MATRIX BIOLOGY, [2000] Jul 19 (5) 481-211. Ref: 46
Journal code: 9432852. ISSN: 1569-1802.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; JOURNAL ARTICLE
General Review; REVIEW
REVIEW, TUTORIAL
LA English

FS Priority Journals
EM [illegible]
ED Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]
AB **Integrins** are essential for the development of the two genetically tractable invertebrate model organisms, the nematode worm Caenorhabditis elegans and the fruit fly Drosophila melanogaster. Just two **integrins** are present in C. elegans: one putative RGD binding **integrin** alphapat-2betapat-3, corresponding to Drosophila alphaPS2betaPS and vertebrate alpha5beta1, alphaVbeta1 and alpha8beta1, and one putative laminin binding **integrin** alphaina-1betapat-3, corresponding to Drosophila alphaPS1betaPS and vertebrate alpha3beta1, alpha6beta1 and **alpha7beta1**. In this review, the function of this minimal set of **integrins** during the development of these two invertebrates is compared. Despite the differences in bodyplan and developmental strategy, **integrin** adhesion to the extracellular matrix is required for similar processes: the formation of the link that **translates** muscle contraction into movement of the exoskeleton, cell migration, and morphogenetic interactions between epithelia. Other **integrin** functions, such as regulation of gene expression, have not yet been experimentally demonstrated in both organisms. Additional proteins have been characterised in each organism that are essential for **integrin** function, including extracellular matrix ligands and intracellular interacting proteins, but so far different proteins have been found in the two organisms. This in part represents the fact that the characterisation of the full set of interacting proteins is not complete in either system. However, in other cases different proteins appear to be used for similar functions in the two animals. The continued use of genetic approaches to identify proteins required for **integrin** function in these two model organisms should lead to the identification of the minimal set of conserved components that form **integrin** adhesive structures.
CT Check Tags: Animal; Human
Caenorhabditis elegans: GE, genetics
Cell Adhesion
Drosophila melanogaster: PH, physiology
Extracellular Matrix: ME, metabolism
Forecasting
Integrins: CL, classification
***Integrins: GE, genetics**
Integrins: PH, physiology
Invertebrates: GE, genetics
Phenotype
Vertebrates: GE, genetics
CN 0 (**Integrins**); 0 (**integrin** PS, Drosophila); 0 (**integrin** betapat-3)

L83 ANSWER 15 OF 45 MEDLINE
AN 2000496259 MEDLINE
DN 20372683 PubMed ID: 10910772
TI Laminin and **alpha7beta1 integrin** regulate agrin-induced clustering of acetylcholine receptors.
AU Burkin D J; Kim J E; Gu M; Kaufman S J
CS Department of Cell and Structural Biology, University of Illinois, Urbana, IL 61801, USA.
SO JOURNAL OF CELL SCIENCE, [illegible] Aug; 113 (Pt 16): 2877-91.
Journal code: [illegible]. ISSN: [illegible].
CY ENGLAND: United Kingdom
DT Journal; Article; JOURNAL ARTICLE
LA English
FS Priority Journals
EM [illegible]

ED Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB The clustering of acetylcholine receptors (AChRs) in the post-synaptic membrane of skeletal muscle is an early developmental event in the formation of the neuromuscular junction. Several studies show that laminin, as well as neural agrin, can induce AChR clustering in C2C12 myofibers. We recently showed that specific isoforms of the **alpha7beta1 integrin** (a receptor normally found at neuromuscular junctions) colocalize and physically interact with AChR clusters in a laminin-dependent fashion. In contrast, induction with agrin alone fails to promote localization of the **integrin** with AChR clusters. Together both agrin and laminin enhance the interaction of the **integrin** with AChRs and their aggregation into clusters. To further understand this mechanism we investigated cluster formation and the association of the **alpha7beta1 integrin** and AChR over time following induction with laminin and/or agrin. Our results show that the **alpha7beta1 integrin** associates with AChRs early during the formation of the post-synaptic membrane and that laminin modulates this recruitment. Laminin induces a rapid stable association of the **integrin** and AChRs and this association is independent of clustering. In addition to laminin-1, merosin (laminin-2/4) is present both before and after formation of neuromuscular junctions and also promotes AChR clustering and colocalization with the **integrin** as well as synergism with agrin. Using site directed mutagenesis we demonstrate that a tyrosine residue in the cytoplasmic domain of both (&agr;)7A and (&agr;)7B chains regulates the localization of the **integrin** with AChR clusters. We also provide evidence that laminin, through its association with the **alpha7beta1 integrin**, reduces by 20-fold the concentration of agrin required to promote AChR clustering and accelerates the formation of clusters. Thus laminin, agrin and the **alpha7beta1 integrin** act in a concerted manner early in the development of the post-synaptic membrane, with laminin priming newly formed myofibers to rapidly and vigorously respond to low concentrations of neural agrin produced by innervating motor neurons.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Agrin: ME, metabolism
*Agrin: PD, pharmacology
Cells, Cultured
Cytoplasm: ME, metabolism
Fluorescent Antibody Technique
Immunoblotting
Integrins: AN, analysis
***Integrins: ME, metabolism**
Laminin: ME, metabolism
*Laminin: PD, pharmacology
Mice
Muscle Fibers: CH, chemistry
Muscle Fibers: CY, cytology
*Muscle Fibers: ME, metabolism
Neuromuscular Junction: ME, metabolism
Protein Binding: DE, drug effects
Receptors, Cholinergic: AN, analysis
*Receptors, Cholinergic: ME, metabolism
Tyrosine: ME, metabolism

RN [illegible]-41-6 (Tyrosine)

CN [illegible] (Agrin) ; [illegible] **Integrins** ; [illegible] (Laminin) ; [illegible] (Receptors, Cholinergic) ; [illegible] **integrin alpha7beta1** ; [illegible] (Laminin 1)

L66 ANSWER 16 OF 48 MEDLINE
AN [illegible] MEDLINE
DN [illegible] PubMed ID: [illegible]

TI Laminin alpha4 and **integrin** alpha6 are upregulated in regenerating dy/dy skeletal muscle: comparative expression of laminin and **integrin** isoforms in muscles regenerating after crush injury.

AU Sorokin L M; Maley M A; Moch H; von der Mark H; von der Mark K; Tadalbert L; Marosi S; Davies M J; McGeachie J K; Grounds M D

CS Interdisciplinary Center for Clinical Research (IZKF), University of Erlangen-Nuremberg, Germany.

SO EXPERIMENTAL CELL RESEARCH, (2000 May 1) 256 (2) 511-14.
Journal code: 0373226. ISSN: 0014-4827.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200005

ED Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000518

AB The expression of laminin isoforms and laminin-binding **integrin** receptors known to occur in muscle was investigated during myogenic regeneration after crush injury. Comparisons were made between dystrophic (129ReJ dy/dy mice, which have reduced laminin alpha2 expression, and their normal littermates. The overall histological pattern of regeneration after crush injury was similar in dy/dy and control muscle, but proceeded faster in dy/dy mice. In vitro studies revealed a greater yield of mononuclear cells extracted from dy/dy muscle and a reduced proportion of desmin-positive cells upon in vitro cultivation, reflecting the presence of inflammatory cells and "preactivated" myoblasts due to ongoing regenerative processes within the endogenous dystrophic lesions. Laminin alpha1 was not detectable in skeletal muscle. Laminin alpha2 was present in basement membranes of mature myofibers and newly formed myotubes in control and dy/dy muscles, albeit weaker in dy/dy. Laminin alpha2-negative myogenic cells were detected in dy/dy and control muscle, suggesting the involvement of other laminin alpha chains in early myogenic differentiation, such as laminin alpha4 and alpha5 which were both transiently expressed in basement membranes of newly formed myotubes of dy/dy and control mice. **Integrin beta1** was expressed on endothelial cells, muscle fibers, and peripheral nerves in uninjured muscle and broadened after crush injury to the interstitium where it occurred on myogenic and nonmyogenic cells. **Integrin** alpha3 was not expressed in uninjured or regenerating muscle, while **integrin** alpha6 was expressed mainly on endothelial cells and peripheral nerves in uninjured muscle. Upon crush injury **integrin** alpha6 increased in the interstitium mainly on nonmyogenic cells, including infiltrating leukocytes, endothelial cells, and fibroblasts. In dy/dy muscle, **integrin** alpha6 occurred on some newly formed myotubes. **Integrin alpha7** was expressed on muscle fibers at the myotendinous junction and showed weak and irregular expression on muscle fibers. After crush injury, **integrin alpha7** expression extended to the newly formed myotubes and some myoblasts. However, many myoblasts and newly formed myotubes were **integrin alpha7** negative. No marked difference was observed in **integrin alpha7** expression between dy/dy and control muscle, either uninjured or after crush injury. Only laminin alpha4 and **integrin** alpha6 expression patterns were notably different between dy/dy and control muscle. Expression of both molecules was more extensive in dy/dy muscle, especially in the interstitium of regenerating areas and on newly formed myotubes. In view of the faster myogenic regeneration observed in dy/dy mice, the data suggest that laminin alpha4 and **integrin** alpha6 support myogenic regeneration. However, whether these accelerated myogenic effects are a direct consequence of the reduced laminin alpha1 expression in dy/dy mice, or an accentuation of the ongoing regenerative events in focal lesions in the muscle, requires further investigation.

CT Check Tags: Animal; Support, Non-U.S. Gov't
*Antigens, CD: ME, metabolism
Fluorescent Antibody Technique
Immunoenzyme Techniques
Integrin alpha3beta1
Integrin alpha6
Integrin alpha6beta1
Integrins: ME, metabolism
*Laminin: ME, metabolism
Mice
Muscle, Skeletal: IN, injuries
*Muscle, Skeletal: ME, metabolism
Muscle, Skeletal: PH, physiology
Protein Isoforms: ME, metabolism
*Regeneration
Up-Regulation
RN 151186-83-2 (Laminin A)
CN 1 (Antigens, CD); 0 (**Integrin** alpha3beta1); 0 (**Integrin** alpha6); 0 (**Integrin** alpha6beta1); 0 (**Integrins**); 0 (Laminin); 0 (Protein Isoforms); 0 (**integrin alpha7beta1**); 0 (laminin alpha 2); 0 (laminin alpha 4); 0 (laminin alpha5)

L83 ANSWER 17 OF 45 MEDLINE
AN **2000175149** MEDLINE
DN **20175149** PubMed ID: **10711985**
TI The childhood **muscular dystrophies**: making order out of chaos.
AU Isaac C Y; Mendell J R
CS Department of Neurology, The Ohio State University, Columbus 43210, USA.
SO SEMINARS IN NEUROLOGY, (1999) 19 (1) 9-23. Ref: 145
Journal code: 8111348. ISSN: 0271-8235.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000331
AB New discoveries have dramatically changed the way we approach and think about patients with childhood **muscular dystrophies**. An aura of order and organization seems to be at hand for a group of diseases which previously seemed endlessly heterogeneous. We have learned that young boys and girls with proximal muscle weakness, large calves and elevated serum CK may have any one of a number of closely connected disorders which affect a complex of interacting proteins of the dystrophin-glycoprotein complex. This complex links the intracellular cytoskeleton to the extracellular matrix. Patients with Duchenne and Becker dystrophies lack dystrophin, while some of the limb girdle **muscular dystrophies** (an archaic term) are deficient in sarcoglycans and other proteins. The concept of interrelated disorders extends to the previously orphaned distal **muscular dystrophies**, or distal myopathies, as they are often called. A surprise finding is that the C. elegans protein, dysferlin, is conserved and expressed in man. We know little of the function of this protein in human primates, but its loss in muscle has brought seemingly disparate disorders together, since both a form of LGMD 2B and distal myopathy (Miyoshi myopathy) are deficient in this same gene product. The congenital **muscular dystrophies** are also well-entrenched in our expanding concepts of underliness of disease. The

defect in the laminin-alpha2 chain, a direct ligand to the dystrophin-glycoprotein complex, causes a form of **muscular dystrophy** which affects infants. Another variant of congenital **muscular dystrophy** is deficient the **integrin alpha7**, an important laminin receptor. Finally, in Fukuyama congenital **muscular dystrophy**, the deficient fukutin gene product may also be linked to the basal lamina, permitting overmigration of neuronal cells which lead to micropolygyria in the brain, and at the same time cause basal lamina defects in the extracellular matrix of skeletal muscle, which leads to **muscular dystrophy**. As we approach the millennium, those of us who have seen the transition from the pre-molecular to the molecular era of myology know that we leave behind a great legacy of chaos (no great loss!), replaced by a foundation for conceptual organization which will serve to establish new roots for research as well as for the enriched practice of medicine. The future looks bright for our field and our patients!

CT Check Tags: Human
Child
Creatine Kinase: BL, blood
Dystrophin: DF, deficiency
Dystrophin: GE, genetics
*Extracellular Matrix Proteins: GE, genetics
Gene Expression Regulation
Gene Therapy
Laminin: DF, deficiency
Laminin: GE, genetics
*Membrane Glycoproteins: GE, genetics
Muscle Contraction
Muscular Dystrophies: CN, congenital
Muscular Dystrophies: GE, genetics
***Muscular Dystrophies: ME, metabolism**
Muscular Dystrophies: PP, physiopathology
Muscular Dystrophies: TH, therapy
Proteins: GE, genetics
Proteins: ME, metabolism
Receptors, Laminin: GE, genetics

CN 0 (Dystrophin); 0 (Extracellular Matrix Proteins); 0 (Laminin); 0 (Membrane Glycoproteins); 0 (Proteins); 0 (Receptors, Laminin); 0 (fukutin); EC 2.7.3.2 (Creatine Kinase)

L83 ANSWER 18 OF 48 MEDLINE
AN 2000160722 MEDLINE
DN 20160722 PubMed ID: 10694445
TI The role of extracellular and cytoplasmic splice domains of **alpha7 -integrin** in cell adhesion and migration on laminins.
AU Schober S; Mielenz D; Echtermeyer F; Hapke S; Poschl E; von der Mark H; Moch H; von der Mark K
CS Institute of Experimental Medicine, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, 91054, Germany.
SO EXPERIMENTAL CELL RESEARCH, [illegible] Mar 15, 255 (2) 303-11.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000315
Last Updated on STN: 20000315
Entered Medline: 20000414
AB The major laminin-binding **integrin** of skeletal, smooth, and heart muscle is **alpha7beta1-integrin**, which is structurally related to alpha6beta1. It occurs in three cytoplasmic splice variants **alpha7A**, -B, and -C and two extracellular

forms M1 and M2 which are developmentally regulated and differentially expressed in skeletal muscle. Previously, we have shown that ectopic expression of the **alpha7beta-integrin** splice variant in nonmotile HEK293 cells specifically induced cell locomotion on laminin-1 but not on fibronectin. To investigate the specificity and the mechanism of the **alpha7**-mediated cell motility, we expressed the three **alpha7**-chain cytoplasmic splice variants, as well as alpha6A- and alpha6B-**integrin** subunits in HEK293 cells. Here we show that all three **alpha7** splice variants (containing the X2 domain), as well as alpha6A and alpha6B, promote cell attachment and stimulate cell motility on laminin-1 and its E8 fragment. Deletion of the cytoplasmic domain (excluding the GFFKR consensus sequence) from **alpha7B** resulted in a loss of the motility-enhancing effect. On laminin-2/4 (merosin), the predominant isoform in mature skeletal muscle, only **alpha7**-expressing cells showed enhanced motility, whereas cells transfected with alpha6A and alpha6B neither attached nor migrated on laminin-2. Adhesion of **alpha7**-expressing cells to both laminin-1 and laminin-2 was specifically inhibited by a new monoclonal antibody (6A11) specific for **alpha7**. Expression of the two extracellular splice variants **alpha7X1** and **alpha7X2** in HEK293 cells conferred different motilities on laminin isoforms: Whereas **alpha7X2B** promoted cell migration on both laminin-1 and laminin-2, **alpha7X1B** supported motility only on laminin-2 and not on laminin-1, although both X1 and X2 splice variants revealed similar adhesion rates to laminin-1 and -2. Fluorescence-activated cell sorter analysis revealed a dramatic reduction of surface expression of alpha6-**integrin** subunits after **alpha7A** or -B transfection; also, surface expression of alpha1-, alpha3-, and alpha6-**integrins** was significantly reduced. These results demonstrate selective responses of alpha6- and **alpha7-integrins** and of the **alpha7** splice variants to laminin-1 and -2 and indicate differential roles in laminin-controlled cell adhesion and migration.

CT Check Tags: Human; Support, Non-U.S. Gov't
*Antigens, CD
Antigens, CD: GE, genetics
Cell Adhesion: GE, genetics
Cell Line
*Cell Movement
Cell Movement: GE, genetics
Integrins: GE, genetics
*Laminin
RNA Splicing
CN 0 (Antigens, CD ; 0 (ITGA7 protein, human); 0 (**Integrins**); 0 (Laminin)

L83 ANSWER 19 OF 45 MEDLINE
AN 2000150162 MEDLINE
DN 20150162 PubMed ID: 10684883
TI Impaired axonal regeneration in **alpha7 integrin** -deficient mice.
AU Werner A; Willem M; Jones L L; Kreutzberg G W; Mayer U; Raivich G
CS Department of Neuromorphology, Max-Planck-Institute of Neurobiology, [illegible] Martinsried, Germany.
SO JOURNAL OF NEUROSCIENCE, [illegible] Mar 1, 20[illegible] 8 1682-91.
Journal code: 8102140. ISSN: 1529-2401.
PY United States
DT Journal; Article; JOURNAL ARTICLE
LA English
FS Priority Journals
EM [illegible]
ED Entered STN: 20000321
Last Updated on STN: 20000621

Entered Medline: 20000113
AB The interplay between growing axons and the extracellular substrate is pivotal for directing axonal outgrowth during development and regeneration. Here we show an important role for the neuronal cell adhesion molecule **alpha7beta1 integrin** during peripheral nerve regeneration. Axotomy led to a strong increase of this **integrin** on regenerating motor and sensory neurons, but not on the normally nonregenerating CNS neurons. **alpha7** and **beta1** subunits were present on the axons and their growth cones in the regenerating facial nerve. Transgenic deletion of the **alpha7** subunit caused a significant reduction of axonal elongation. The associated delay in the reinnervation of the whiskerpad, a peripheral target of the facial motor neurons, points to an important role for this **integrin** in the successful execution of axonal regeneration.
CT Check Tags: Animal; Support, Non-U.S. Gov't
*Antigens, CD: BE, genetics
*Axons: PH, physiology
Axotomy
Facial Nerve: CY, cytology
Facial Nerve: PH, physiology
Facial Nerve Injuries: PP, physiopathology
Gene Expression: PH, physiology
Growth Cones: PH, physiology
Growth Cones: UL, ultrastructure
Mice
Mice, Inbred C57BL
Mice, Knockout
Microscopy, Electron
Motor Neurons: PH, physiology
Motor Neurons: UL, ultrastructure
*Nerve Regeneration: PH, physiology
Neuroglia: PH, physiology
CN 0 (Antigens, CD); 0 (ITGA7 protein, human)

L83 ANSWER 20 OF 45 MEDLINE
AN 20000061955 MEDLINE
DN 20061955 PubMed ID: 10616209
TI Organization of the myotendinous junction is dependent on the presence of **alpha7beta1 integrin**.
AU Mayer U; Klenczar C; Herken R; Willem M; Mayer U
CS Zentrum Anatomie, Abteilung Histologie, Universitat Gottingen, Germany.. mmayer@gwdg.de
SO LABORATORY INVESTIGATION, (1999 Dec) 79 (12) 1591-9.
Journal code: 0376617. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000113
AB The laminin receptor **alpha7beta1** is enriched at the myotendinous junctions, and mice with a targeted inactivation of the **alpha7** gene develop a form of **muscular dystrophy** that primarily affects this structure. By ultrastructural analysis of **alpha7**-deficient mice, in comparison with wild-type and mdx mice, we attempted to elucidate the role of **alpha7 integrin** for the integrity and function of the myotendinous junctions. Ultrastructurally, myotendinous junctions of **alpha7**-deficient myofibers lose their interdigitations and the myofilaments detract from the sarcolemmal membrane, whereas the lateral side of the myofibers remains morphologically normal. The basement membrane at the myotendinous

functions in **alpha7** - - mice is significantly broadened, and immunogold-histochemistry has demonstrated that the laminin alpha1 chain is not localized here but, instead, in the matrix of the neighboring tendon. In contrast, mdm mice have normal myotendinous functions, with a matrix protein pattern also found in wild-type mice, however the lateral sides of the myofibers are severely damaged. These results suggest that the **alpha7beta1 integrin** is a major receptor connecting the muscle cell to the tendon and helps to organize the myotendinous junction, whereas the dystrophin-glycoprotein complex is necessary for the lateral integrity of the muscle cell.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Basement Membrane: UL, ultrastructure
Immunohistochemistry
Integrins: GE, genetics
***Integrins: ME, metabolism**
Mice
Mice, Inbred mdx
Mice, Knockout
Microscopy, Electron
Muscle, Skeletal: ME, metabolism
*Muscle, Skeletal: UL, ultrastructure
Tendons: ME, metabolism
*Tendons: UL, ultrastructure

CN 0 (**Integrins** ;) (**integrin alpha7beta1**)

L83 ANSWER 21 OF 45 MEDLINE
AN 1999364627 MEDLINE
DN 99364627 PubMed ID: 10437916
TI Expression of the **alpha7beta1** laminin receptor suppresses melanoma growth and metastatic potential.
AU Zieber B L; Chen Y Q; Ramos D M; Waleh N; Kramer R H
CS Department of Stomatology, University of California San Francisco, 94143, USA.
NC DE 11911 (NIDCR)
DE 13479 (NIDCR)
SO CELL GROWTH AND DIFFERENTIATION, (1999 Jul) 10 (7) 479-90.
Journal code: 9100024. ISSN: 1044-9523.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990925
Last Updated on STN: 20000303
Entered Medline: 19990914

AB The **alpha7beta1 integrin** is a laminin-binding receptor that was originally identified in melanoma. Here, we show that, in clonally derived mouse K1735 melanoma variant cell lines with high (M-2) and low (C-23) metastatic potential, elevated expression of **alpha7** correlates with reduced cell motility, metastasis, and tumor growth. Both cell lines showed similar **beta1 integrin**-dependent adhesion to laminin-1 and the E8 laminin fragment. However, the highly metastatic M-2 cells rapidly migrated on laminin, whereas the nonmetastatic C-23 cells were minimally motile. Laminin-binding **integrin** profiles showed that the M-2 cells expressed moderate amounts of alpha1 and abundant alpha6 but low or undetectable levels of alpha2 and **alpha7**. By contrast, C-23 cells expressed low or undetectable levels of alpha1, alpha2, and alpha6 but had up-regulated levels of **alpha7**. Consistent with the protein data, Northern blot analysis showed that levels of **alpha7** mRNA were highest in the poorly metastatic variant cells, whereas alpha6 message was not detected; in contrast, alpha6 mRNA was elevated in the highly metastatic cells, whereas **alpha7** message was not detected. Forced

expression of **alpha7** in the M-1 cells suppressed cell motility, tumor growth, and metastasis. Collectively, these results indicate that, during melanoma progression, acquisition of a highly tumorigenic and metastatic melanoma phenotype is associated with loss of the **alpha7beta1** laminin receptor.

DT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cell Adhesion
Cell Movement
Integrins: GE, genetics
***Integrins: ME, metabolism**
Laminin: ME, metabolism
Melanoma, Experimental: GE, genetics
Melanoma, Experimental: ME, metabolism
*Melanoma, Experimental: PA, pathology
Mice
Mice, Inbred C3H
Mice, Nude
Neoplasm Metastasis
Neoplasm Transplantation
Receptors, Laminin: GE, genetics
*Receptors, Laminin: ME, metabolism
Transcription, Genetic
Tumor Cells, Cultured

CN 0 (**Integrins**); 0 (Laminin); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

L83 ANSWER 22 OF 45 MEDLINE
AN 1999297485 MEDLINE
DN 99297485 PubMed ID: 10371075
TI Secondary reduction of **alpha7B integrin** in laminin alpha2 deficient congenital **muscular dystrophy** supports an additional transmembrane link in skeletal muscle.
AU Ehmsen P D; Mayer U; Saher G; Herrmann R; van der Flier A; Sonnenberg A; Sorokin L; Voit T
CS Department of Pediatrics, University of Essen, Germany.
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, (1999 Mar 1) 163 (2) 140-52.
Journal code: 0375403. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 19990806
Last Updated on STN: 20020212
Entered Medline: 19990723
AB The **integrins** are a large family of heterodimeric transmembrane cellular receptors which mediate the association between the extracellular matrix (ECM) and cytoskeletal proteins. The **alpha7beta1 integrin** is a major laminin binding **integrin** in skeletal and cardiac muscle and is thought to be involved in myogenic differentiation and migration processes. The main binding partners of the **alpha7 integrin** are laminin-1 (**alpha1-beta1**-gamma1), laminin-2 (**alpha2-beta1**-gamma1) and laminin-4 (**alpha2-beta2**-gamma1). Targeted deletion of the gene for the **alpha7 integrin** subunit ("ITGA7") in mice leads to a novel form of **muscular dystrophy**. In the present study we have investigated the expression of two alternative splice variants, the **alpha7B** and beta1B **integrin** subunits, in normal human skeletal muscle, as well as in various forms of **muscular dystrophy**. In normal human skeletal muscle the expression of the **alpha7 integrin** subunit appeared to be developmentally regulated: it was first detected at 2 years of age. In contrast, the beta1 **integrin** could be detected in immature and mature muscle

in the sarcolemma of normal fetal skeletal muscle at 12 weeks gestation. The expression of **alpha7B integrin** was significantly reduced at the sarcolemma in six patients with laminin alpha2 chain deficient congenital **muscular dystrophy** (CMD; age <2 years). However, this reduction was not correlated with the amount of laminin alpha2 chain expressed. In contrast, the expression of the laminin alpha2 chain was not altered in the skeletal muscle of the **alpha7** knock-out mice. These data argue in favor that there is not a tight correlation between the expression of the **alpha7 integrin** subunit and that of the laminin alpha2 chain in either human or murine dystrophic muscle. Interestingly, in dystrophinopathies (Duchenne and Becker **muscular dystrophy**; DMD/BMD) expression of **alpha7B** was upregulated irrespective of the level of dystrophin expression as shown by a strong sarcolemmal staining pattern even in young boys (age <2 years). The expression of the beta1D **integrin** subunit was not altered in any of our patients with different types of **muscular dystrophy**. In contrast, sarcolemmal expression of beta1D **integrin** was significantly reduced in the **alpha7 integrin** knock-out mice, whereas the expression of the components of the DGC was not altered. The secondary loss of **alpha7B** in laminin alpha2 chain deficiency defines a biochemical change in the composition of the plasma membrane resulting from a primary protein deficiency in the basal lamina. These findings, in addition to the occurrence of a **muscular dystrophy** in **alpha7** deficient mice, implies that the **alpha7B integrin** is an important laminin receptor within the plasma membrane which plays a significant role in skeletal muscle function and stability.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Adolescent
Adult
Aging
Amino Acid Sequence
Antibodies
*Antigens, CD: GE, genetics
Antigens, CD: PH, physiology
Child
Child, Preschool
Cytoskeletal Proteins: GE, genetics
Dystrophin: GE, genetics
Embryo and Fetal Development
Fetus
Gene Expression Regulation, Developmental
Infant
Infant, Newborn
Integrins: GE, genetics
*Laminin: DF, deficiency
*Laminin: GE, genetics
Membrane Glycoproteins: GE, genetics
Mice
Mice, Knockout
Molecular Sequence Data
Muscle Development
Muscle, Skeletal: EM, embryology
Muscle, Skeletal: GE, growth & development
*Muscle, Skeletal: PP, physiopathology
Muscular Dystrophies: CN, congenital
***Muscular Dystrophies: GE, genetics**
Protein Isoforms: GE, genetics
RN 146668-27-9 (43-156K dystrophin-associated glycoprotein)
CN [illegible] Antibodies ; [illegible] Antigens, CD ; [illegible] Cytoskeletal Proteins ; [illegible] Dystrophin ; [illegible] ITGA7 protein, human ; [illegible] **Integrins** ; [illegible] Laminin ; [illegible] Membrane Glycoproteins ; [illegible] Protein Isoforms ; [illegible] adhalin ;

? laminin alpha 2

L83 ANSWER 23 OF 45 MEDLINE
AN 1999242615 MEDLINE
DN 99242615 PubMed ID: 10228961
TI Laminin polymerization induces a receptor-cytoskeleton network.
AU Colognato H; Winkelmann D A; Yurchenco P D
CS Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Piscataway, New Jersey 08854, USA.
NC R01-AR38454 (NIAMS)
R01-DK36425 (NIDDK)
SO JOURNAL OF CELL BIOLOGY, (1999 May 3) 145 (3) 619-31.
Journal code: 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990614
Last Updated on STN: 19990614
Entered Medline: 19990601
AB The transition of laminin from a monomeric to a polymerized state is thought to be a crucial step in the development of basement membranes and in the case of skeletal muscle, mutations in laminin can result in severe **muscular dystrophies** with basement membrane defects. We have evaluated laminin polymer and receptor interactions to determine the requirements for laminin assembly on a cell surface and investigated what cellular responses might be mediated by this transition. We found that on muscle cell surfaces, laminins preferentially polymerize while bound to receptors that included dystroglycan and **alpha7beta1 integrin**. These receptor interactions are mediated through laminin COOH-terminal domains that are spatially and functionally distinct from NH2-terminal polymer binding sites. This receptor-facilitated self-assembly drives rearrangement of laminin into a cell-associated polygonal network, a process that also requires actin reorganization and tyrosine phosphorylation. As a result, dystroglycan and **integrin** redistribute into a reciprocal network as do cortical cytoskeleton components vinculin and dystrophin. Cytoskeletal and receptor reorganization is dependent on laminin polymerization and fails in response to receptor occupancy alone (nonpolymerizing laminin). Preferential polymerization of laminin on cell surfaces, and the resulting induction of cortical architecture, is a cooperative process requiring laminin- receptor ligation, receptor-facilitated self-assembly, actin reorganization, and signaling events.
CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Actins: ME, metabolism
Cells, Cultured
Cytoskeleton: CH, chemistry
*Cytoskeleton: ME, metabolism
***Integrins: ME, metabolism**
*Laminin: CH, chemistry
*Laminin: ME, metabolism
Membrane Proteins: CH, chemistry
Membrane Proteins: ME, metabolism
Mice
Mice, Mutant Strains
Muscle, Skeletal: CY, cytology
Muscular Dystrophy, Animal: ME, metabolism
Phosphorylation
Polymers
Protein Structure, Tertiary
Receptors, Laminin: ME, metabolism
Sarcolemma: CH, chemistry

Sarcolemma: ME, metabolism
Tyrosine: ME, metabolism
RN 60-41-6 (Tyrosine)
CN 1 (Antigens); 2 (**Integrins**); 3 (Laminin); 4 (Membrane Proteins); 5 (Polymers); 6 (Receptors, Laminin); 7 (**integrin alpha7beta1**); 8 (laminin alpha 2)

L63 ANSWER 24 OF 45 MEDLINE
AN **1999238963** MEDLINE
DN **99238963** PubMed ID: **10222457**
TI Merosin-positive congenital **muscular dystrophy**: a large inbred family.
AU Mahjneh I; Bushby K; Anderson L; Muntoni F; Tolvanen-Mahjneh H; Bashir R; Pizzi A; Brockington M; Marconi G
CS Department of Neurological and Psychiatric Sciences, University of Florence, Italy.
SO NEUROPEDIATRICS, (1999 Feb) 30 (1) 22-8.
Journal code: 8102187. ISSN: 0174-304X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990623
Last Updated on STN: 20000303
Entered Medline: 19990615
AB Large families with congenital **muscular dystrophy** are rare. We report a clinical, histopathological, immunocytochemical, electrophysiological, radiological and genetic study of 10 cases affected by "pure" CMD belonging to two generations of a large inbred Palestinian family. The disease showed autosomal recessive inheritance. All patients had generalised muscular weakness and hypotonia at birth without arthrogryposis. They had a relatively benign clinical course with stabilisation of the clinical picture at different ages and at variable degrees of severity. The pattern of muscle weakness and wasting was more marked in the proximal upper limb-girdle and trunk muscles. Lower limb muscles were more mildly involved. Serum CK was normal or moderately increased. All patients had normal intelligence, normal computed tomography (CT) scans of the brain and normal somatosensory evoked potentials (SEP). Electromyography (EMG) and muscle **biopsy** showed morphological changes compatible with **muscular dystrophy**. Immunocytochemistry for dystrophin, laminin alpha 2 of merosin, and for alpha, beta, gamma sarcoglycans was normal. Linkage analysis excluded all the known loci for CMD, including laminin alpha 2 on chromosome 6q2, the Fukuyama congenital **muscular dystrophy** locus on 9q3, the **integrin alpha 7** locus on chromosome 12q13 and the recently identified locus on 1p35-36. The family we present is clinically and genetically distinct from the already mapped forms of congenital **muscular dystrophy**. Genetic studies are in progress to localise the gene responsible for this condition.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adolescent
Adult
Biopsy
Child
Child, Preschool
*Chromosome Mapping
Consanguinity
Immunohistochemistry
Infant
Israel: EH, ethnology
*Laminin: GE, genetics

London
Muscle Hypotonia: ET, etiology
*Muscles: PA, pathology
Muscular Dystrophies: CO, complications
*Muscular Dystrophies: CN, congenital
Muscular Dystrophies: DI, diagnosis
*Muscular Dystrophies: GE, genetics
Pedigree
CN 0 (Laminin)

L83 ANSWER 25 OF 48 MEDLINE
AN 1999216351 MEDLINE
DN 99216351 PubMed ID: 10199978
TI The **alpha7beta1 integrin** in muscle development and disease.
AU Burkin D J; Kaufman S J
CS Department of Cell and Structural Biology, University of Illinois, B107 Chemical and Life Sciences Laboratory, Urbana, IL 61801, USA.
SO CELL AND TISSUE RESEARCH, (1999 Apr) 296 (1) 183-90. Ref: 43
Journal code: 0417625. ISSN: 0302-766X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990517
AB The **alpha7beta1 integrin** is a laminin receptor on the surface of skeletal myoblasts and myofibers. Alternative forms of both the **alpha7** and **beta1** chains are expressed in a developmentally regulated fashion during myogenesis. These different **alpha7beta1** isoforms localize at specific sites on myofibers and appear to have distinct functions in skeletal muscle. These functions include the migration and proliferation of developing myoblasts, the formation and integrity of neuromuscular and myotendinous junctions, and the "gluing" together of muscle fibers that is essential to the generation of contractile force. The **alpha7beta1 integrin** appears to be both directly and indirectly causally related to several muscle diseases. Enhanced expression of **alpha7beta1**-mediated linkage of the extracellular matrix is seen in Duchenne **muscular dystrophy** and may compensate for the absence of the dystrophin-mediated linkage. Downregulation of expression of the **integrin** may contribute to the development of pathology in congenital laminin deficiencies. Mutations in the **alpha7 integrin** gene underlie additional congenital muscle diseases. The functional roles of this **integrin** in the formation and stability of the neuromuscular and myotendinous junctions and its localization between fibers suggest that altered expression or function of this **integrin** may have widespread involvement in other myopathies. The localization of the **alpha7** gene at human chromosome 12q13 is a useful clue for focusing such studies.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Chromosome Mapping
Chromosomes, Human, Pair 12
Integrins: GE, genetics
*Integrins: PH, physiology
Models, Biological
Muscle Fibers: CY, cytology
*Muscle Fibers: PH, physiology

Muscle, Skeletal: EM, embryology
*Muscle, Skeletal: PH, physiology
Muscle, Skeletal: PP, physiopathology
Neuromuscular Diseases: GE, genetics
*Neuromuscular Diseases: PP, physiopathology
Neuromuscular Junction: PH, physiology
CN 2 (**Integrins**); 1 (**integrin alpha7beta1**)

L83 ANSWER 26 OF 45 MEDLINE
AN **1999151804** MEDLINE
DN **99151804** PubMed ID: **10029346**
TI A novel form of familial congenital **muscular dystrophy** in two adolescents.
AU Salih M A; Al Rayess M; Dutshall S; Urtizberea J A; Al-Turaiki M H; Ozo C O; Straub V; Akbar M; Abid M; Andeejani A; Campbell K P
CS Department of Pediatrics, College of Medicine, King Saud University, Riyadh, Saudi Arabia.
SO NEUROPEDIATRICS, (1998 Dec) 29 (6) 289-93.
Journal code: 8101187. ISSN: 0174-304X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990507
Last Updated on STN: 20000303
Entered Medline: 19990524
AB We report on two brothers (the product of first-degree consanguineous marriage; aged 15 and 12 years) who presented with severe hypotonia at birth, proximal muscle weakness associated with delayed motor milestones but normal cognitive function. Investigations (at 4 years of age) revealed mildly elevated serum creatine kinase (CK) levels (300 and 824 IU/l; N < or = 210). Muscle **biopsies** showed minimal change myopathy, no neurogenic atrophy but remarkable type-1 fibre predominance (up to 85.5%) without fibre-type disproportion. Clinical examination at 12 and 9 years, respectively, showed mild facial weakness and high-arched palate in both patients. The younger sibling also had ptosis but otherwise normal external ocular muscles. They showed symmetric proximal muscle weakness and wasting associated with calf-muscle hypertrophy. They could walk independently. A repeat muscle **biopsy** showed advanced dystrophic changes in the younger patient at the age of 10 years. Virtually all the remaining fibres were type 1. Immunohistochemistry revealed normal expression of the dystrophin-glycoprotein complex (DGC), including dystrophin, beta-dystroglycan, alpha-(adhalin), beta-, gamma-, and delta-sarcoglycan, laminin-alpha2 chain (merosin) and syntrophin. Mild dystrophic features and type-1 fibre predominance (92.5%) were seen in the **biopsy** of the older patient, whereas immunohistochemistry showed normal expression of the DGC. Both cases also showed clear expression of **integrin alpha7** at the muscle fibre surface and in the blood vessels. Three years later, they could still walk, but with difficulty, and the older brother showed enlargement of the tongue and echocardiographic features of left ventricular dilated cardiomyopathy.
CT Check Tags: Case Report; Human; Male
Adolescent
Child
Child, Preschool
***Consanguinity**
Disease Progression
Dystrophin: AN, analysis
Laminin: AN, analysis
Muscle, Skeletal: CH, chemistry
Muscle, Skeletal: PA, pathology

***Muscular Dystrophies: CN, congenital**
Muscular Dystrophies: GE, genetics
Muscular Dystrophies: PA, pathology
Ventricular Dysfunction, Left: ET, etiology
CN 0 (Dystrophin); 0 (Laminin)

L83 ANSWER 27 OF 45 MEDLINE
AN 1999126400 MEDLINE
DN 99126400 PubMed ID: 9925758
TI The muscle-specific laminin receptor **alpha7 beta1 integrin** negatively regulates alpha5 **beta1** fibronectin receptor function.
AU Tomatis D; Echtermayer F; Schober S; Balzac F; Retta S F; Silengo L; Tarone G
CS Dipartimento di Genetica, Biologia e Biochimica, Universita di Torino, Turin, 10126, Italy.
SO EXPERIMENTAL CELL RESEARCH, (1999 Feb 1) 246 (2) 421-32.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990318
AB **alpha7 beta1** is the major **integrin** complex expressed in differentiated muscle cells where it functions as a laminin receptor. In this work we have expressed the **alpha7 integrin** subunit in CHO cells to investigate the functional properties of this receptor. After transfection with **alpha7** CHO cells acquired the ability to adhere and spread on laminin 1 consistent with the laminin receptor activity of the **alpha7 beta1**. **alpha7** transfectants, however, showed a 70% reduction in the ability to adhere to fibronectin and were unable to assemble a fibronectin matrix. The degree of reduction was inversely related to the level of **alpha7** expression. To define the mechanisms underlying this adhesive defect we analyzed surface expression and functional properties of the alpha5 **beta1** fibronectin receptor. Although cell surface expression of alpha5 **beta1** was reduced by a factor of 20-25% in **alpha7** transfectants compared to control untransfected cells, this slight reduction was not sufficient to explain the dramatic reduction in cell adhesion (70%) and matrix assembly (close to 100%). Binding studies showed that the affinity of 125I-fibronectin for its surface receptor was decreased by 80% in **alpha7** transfectants, indicating that the alpha5 **beta1 integrin** is partially inactivated in these cells. Inactivation can be reversed by Mn2+, a cation known to increase **integrin** affinity for their ligands. In fact, incubation of cells with Mn2+ restored fibronectin binding affinity, adhesion to fibronectin, and assembly of fibronectin matrix in **alpha7** transfectants. These data indicate that **alpha7** expression leads to the functional down regulation of alpha5beta1 **integrin** by decreasing ligand binding affinity and surface expression. In conclusion, the data reported establish the existence of a negative cooperativity between **alpha7** and alpha5 **integrins** that may be important in determining functional regulation of **integrins** during myogenic differentiation.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
CHO Cells
Cell Adhesion
Cell Differentiation

Cell Line
Gene Expression
Hamsters
Integrins: GE, genetics
***Integrins: ME, metabolism**
Manganese
Models, Biological
Molecular Sequence Data
Muscles: CY, cytology
*Muscles: ME, metabolism
Rabbits
*Receptors, Fibronectin: ME, metabolism
Receptors, Laminin: GE, genetics
*Receptors, Laminin: ME, metabolism
Transfection
RN 7439-96-5 (Manganese)
CN 0 (**Integrins**); 0 (Receptors, Fibronectin); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**); 0 (**integrin** alphavbeta1)

L83 ANSWER 28 OF 45 MEDLINE
AN 1999034595 MEDLINE
DN 99034595 PubMed ID: 9817762
TI A functional role for specific spliced variants of the **alpha7beta1 integrin** in acetylcholine receptor clustering.
AU Burkin D J; Gu M; Hodges B L; Campanelli J T; Kaufman S J
CS Department of Cell and Structural Biology, University of Illinois, Urbana, Illinois 61801, USA.
SO JOURNAL OF CELL BIOLOGY, (1998 Nov 16) 143 (4) 1067-75.
Journal code: 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981221
AB The clustering of acetylcholine receptors (AChR) on skeletal muscle fibers is an early event in the formation of neuromuscular junctions. Recent studies show that laminin as well as agrin can induce AChR clustering. Since the **alpha7beta1 integrin** is a major laminin receptor in skeletal muscle, we determined if this **integrin** participates in laminin and/or agrin-induced AChR clustering. The alternative cytoplasmic domain variants, **alpha7A** and **alpha7B**, and the extracellular spliced forms, **alpha7X1** and **alpha7X2**, were studied for their ability to engage in AChR clustering. Immunofluorescence microscopy of C2C12 myofibers shows that the **alpha7beta1 integrin** colocalizes with laminin-induced AChR clusters and to a much lesser extent with agrin-induced AChR clusters. However, together laminin and agrin promote a synergistic response and all AChR colocalize with the **integrin**. Laminin also induces the physical association of the **integrin** and AChR. High concentrations of anti-**alpha7** antibodies inhibit colocalization of the **integrin** with AChR clusters as well as the enhanced response promoted by both laminin and agrin. Engaging the **integrin** with low concentrations of anti-**alpha7** antibody initiates cluster formation in the absence of agrin or laminin. Whereas both the **alpha7A** and **alpha7B** cytoplasmic domain variants cluster with AChR, only those isoforms containing the **alpha7X2** extracellular domain were active. These results demonstrate that the **alpha7beta1 integrin** has a physiologic role in laminin-induced AChR clustering, that alternative

splicing is integral to this function of the **alpha7** chain, and that laminin, agrin, and the **alpha7beta1 integrin** interact in a common or convergent pathway in the formation of neuromuscular junctions.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Agrin: CH, chemistry
Agrin: PH, physiology
*Alternative Splicing: PH, physiology
Antibodies
Cells, Cultured
Fluorescent Antibody Technique
*Integrins: GE, genetics
Integrins: IM, immunology
Laminin: CH, chemistry
Laminin: PH, physiology
Mice
*Muscle Fibers: CH, chemistry
Muscle Fibers: CY, cytology
Muscle Fibers: PH, physiology
Neuromuscular Junction: CH, chemistry
Neuromuscular Junction: PH, physiology
Precipitin Tests
Receptors, Cholinergic: CH, chemistry
*Receptors, Cholinergic: ME, metabolism

CN (Agrin); 0 (Antibodies); 0 (**Integrins**); 0 (Laminin); 0 (Receptors, Cholinergic); 0 (**integrin alpha7beta1**)

L83 ANSWER 19 OF 45 MEDLINE
AN 1998:02188 MEDLINE
DN 98020188 PubMed ID: 9638332
TI Down-regulation of laminin-binding **integrins** by 1 alpha,25-dihydroxyvitamin D3 in human melanoma cells in vitro.
AU Hansen C M; Madsen M W; Arensbak B; Skak-Nielsen T; Latini S; Binderup L
CS Department of Biochemistry, Leo Pharmaceutical Products, Ballerup, Denmark.
SO CELL ADHESION AND COMMUNICATION, (1998 Mar) 5 (2) 109-20.
Journal code: 9417027. ISSN: 1061-5385.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English.
FS Priority Journals
EM 199809
ED Entered STN: 19981006
Last Updated on STN: 20000303
Entered Medline: 19980923
AB In the present investigation the effect of 1 alpha,25(OH)2D3 on the expression of the **integrin** laminin receptor on the melanoma cell line SK-MEL-28 has been examined. The SK-MEL-28 cells were shown to contain high-affinity receptors for 1 alpha,25(OH)2D3 and cell proliferation was found to be inhibited in a dose-dependent manner in response to the hormone. Using monoclonal antibodies against the alpha 6-sub-unit of the **integrin** laminin receptor, immunocytochemistry demonstrated that exposure of cells to 1 alpha,25(OH)2D3 for 5 days caused a reduced staining intensity. This observation was further confirmed by dot blot analysis, where a dose-dependent decline of alpha 6 expression was obtained after treatment of the cells with 1 alpha,25(OH)2D3 for 4 days. FACS-analysis was performed in order to quantify this decline, and it was found that the level of alpha 6-subunits on the cell surface was reduced by more than 40%. Additional investigations including Northern blot analyses of poly(A+)RNA extracts also showed a dose-dependent reduction of alpha 6 mRNA. Interestingly, the decrease of alpha 6 expression on the surface of SK-MEL-28 melanoma cells was accompanied by a reduced ability of the cells to adhere to an artificial basement membrane.

In conclusion, the present investigation shows that besides having an antiproliferative effect on the SK-MEL-28 melanoma cells, 1 alpha,25(OH)2D3 is also able to inhibit the surface expression of the alpha 6-subunit of the **integrin** laminin receptor. Moreover, the results strongly indicate that 1 alpha,25(OH)2D3 exerts its regulatory effect on the alpha 6-subunit at the **transcriptional** level rather than at the protein level.

CT Check Tags: Human
*Antigens, CD: BI, biosynthesis
Antigens, CD: GE, genetics
*Antigens, Surface: BI, biosynthesis
Antigens, Surface: GE, genetics
*Antineoplastic Agents: PD, pharmacology
*Calcitriol: PD, pharmacology
Cell Division: DE, drug effects
***Gene Expression Regulation, Neoplastic: DE, drug effects**
*Growth Inhibitors: PD, pharmacology
Integrin alpha6
Integrin alpha6beta1
Integrin alpha6beta4
***Integrins: BI, biosynthesis**
Integrins: GE, genetics
*Laminin: ME, metabolism
*Melanocytes: DE, drug effects
Melanocytes: ME, metabolism
*Melanoma: PA, pathology
*Neoplasm Proteins: BI, biosynthesis
Neoplasm Proteins: GE, genetics
RNA, Messenger: BI, biosynthesis
RNA, Neoplasm: BI, biosynthesis
Receptors, Calcitriol: ME, metabolism
*Receptors, Laminin: BI, biosynthesis
Receptors, Laminin: GE, genetics
Tumor Cells, Cultured
*Tumor Stem Cells: DE, drug effects
Tumor Stem Cells: ME, metabolism

RN 32222-06-3 (Calcitriol)

CN 0 (Antigens, CD); 0 (Antigens, Surface); 0 (Antineoplastic Agents); 0 (Growth Inhibitors); 0 (**Integrin** alpha6); 0 (**Integrin** alpha6beta1); 0 (**Integrin** alpha6beta4); 0 (**Integrins**); 0 (Laminin); 0 (Neoplasm Proteins); 0 (RNA, Messenger); 0 (RNA, Neoplasm); 0 (Receptors, Calcitriol); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

L83 ANSWER 30 OF 45 MEDLINE
AN **1998250181** MEDLINE
DN **98250181** PubMed ID: **9590299**
TI Mutations in the **integrin alpha7** gene cause congenital myopathy.
AU Hayashi Y K; Chou F L; Engvall E; Ogawa M; Matsuda C; Hirabayashi S; Yokochi K; Ziober B L; Kramer R H; Kaufman S J; Ozawa E; Goto Y; Nonaka I; Tsukahara T; Wang J Z; Hoffman E P; Arahata K
CS Department of Neuromuscular Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Tokyo, Japan.
NC AG 14682 (NIA)
R01 29525
SO NATURE GENETICS, 1998 May, 19 (1), 94-7.
Journal code: 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; JOURNAL ARTICLE
LA English
FS Priority Journals
OS GENBANK-AF052091; GENBANK-U23422

EM 199805
ED Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980529
AB The basal lamina of muscle fibers plays a crucial role in the development and function of skeletal muscle. An important laminin receptor in muscle is **integrin alpha7beta1D**. **Integrin beta1** is expressed throughout the body, while **integrin alpha7** is more muscle-specific. To address the role of **integrin alpha7** in human muscle disease, we determined **alpha7** protein expression in muscle **biopsies** from 117 patients with unclassified congenital myopathy and congenital **muscular dystrophy** by immunocytochemistry. We found three unrelated patients with **integrin alpha7** deficiency and normal laminin alpha2 chain expression. To determine if any of these three patients had mutations of the **integrin alpha7** gene, ITGA7, we cloned and sequenced the full-length human ITGA7 cDNA, and **screened** the patients for mutations. One patient had splice mutations on both alleles; one causing a 21-bp insertion in the conserved cysteine-rich region, and the other causing a 98-bp deletion. A second patient was a compound heterozygote for the same 98-bp deletion, and had a 1-bp frame-shift deletion on the other allele. A third showed marked deficiency of ITGA7 mRNA. Clinically, these patients showed congenital myopathy with delayed motor milestones. Our results demonstrate that mutations in ITGA7 are involved in a form of congenital myopathy.
CT Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antigens, CD: GE, genetics
Base Sequence
Child
Child, Preschool
Cloning, Molecular
DNA, Complementary
Infant
Molecular Sequence Data
Muscle, Skeletal: ME, metabolism
*Muscular Diseases: CN, congenital
*Muscular Diseases: GE, genetics
*Mutation
Polymerase Chain Reaction
RNA, Messenger: GE, genetics
CN 0 (Antigens, CD); 0 (DNA, Complementary); 0 (ITGA7 protein, human); 0 (RNA, Messenger)

L83 ANSWER 31 OF 45 MEDLINE
AN 1998233460 MEDLINE
DN 98233460 PubMed ID: 9570924
TI Interaction of **integrin alpha 7 beta 1** in C2C12 myotubes and in solution with laminin.
AU Zolkiewska A; Thompson W C; Moss J
CS Pulmonary-Critical Care Medicine Branch, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland 20892-1590, USA.
SO EXPERIMENTAL CELL RESEARCH, 1998 Apr 15, 241 (1), 86-94.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; JOURNAL ARTICLE
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980521
Last Updated on STN: 19980521
Entered Medline: 19980514

AB The human **integrin alpha 7** and **beta 1** is a major laminin-binding receptor in skeletal muscle. We studied interactions of **integrin alpha 7 beta 1** with the extracellular matrix protein laminin in solution and in intact cells. **Integrin alpha 7 beta 1** bound to EHS laminin (laminin-1, composed of alpha 1, **beta 1**, and gamma 1 chains), but not to endogenous laminin expressed in C2C12 myotubes. Northern blot analysis demonstrated that C2C12 myotubes synthesized laminin-1 alpha, beta, and gamma subunits mRNAs. C2C12 laminin was, however, immunologically distinct from EHS laminin; it was not recognized by 5D3 anti-laminin-1 monoclonal antibody, whereas 5A2 and LT3 antibodies reacted equally well with C2C12 and EHS laminins. Following deglycosylation of EHS laminin, separation of the subunits by SDS-PAGE, Western blotting, and partial amino acid sequencing of the protein bands, the epitope recognized by 5D3 antibody was localized to the gamma 1 laminin chain. Following binding in vitro, the complex of EHS laminin and **integrin alpha 7 beta 1** was subject to chemical cross-linking. The two proteins did not undergo cross-linking at the cell surface, consistent with the fact that in intact, resting myotubes **integrin alpha 7 beta 1** interacted poorly with EHS laminin, which may reflect a limited accessibility of **integrin alpha 7 beta 1** in the membrane to laminin or an inactive state of the **integrin.**

CT Check Tags: Animal
Amino Acid Sequence
Antibody Specificity
Detergents
Epitopes: DE, drug effects
Epitopes: IM, immunology
Integrins: GE, genetics
Integrins: IM, immunology
***Integrins: ME, metabolism**
Laminin: GE, genetics
Laminin: IM, immunology
*Laminin: PD, pharmacology
Membrane Proteins: IP, isolation & purification
Mice
Molecular Sequence Data
Muscle, Skeletal: CH, chemistry
*Muscle, Skeletal: CY, cytology
*Muscle, Skeletal: ME, metabolism
Protein Binding
RNA, Messenger: AN, analysis
Receptors, Laminin: GE, genetics
Receptors, Laminin: IM, immunology
*Receptors, Laminin: ME, metabolism
Solubility

CN 0 (Detergents); 0 (Epitopes); 0 (**Integrins**); 0 (Laminin); 0 (Membrane Proteins); 0 (RNA, Messenger); 0 (Receptors, Laminin); 1 **integrin alpha7beta1**)

LA ANSWER 32 OF 49 MEDLINE
AN [illegible] MEDLINE
DN [illegible] PubMed ID: 9427295
TI Altered expression of the **alpha7beta1 integrin** in human and murine **muscular dystrophies.**
AU Hodges B L; Hayashi Y K; Nonaka I; Wang W; Arahata K; Kaufman S J
CS Department of Cell and Structural Biology, University of Illinois, Urbana, USA.
NC AR44602 NIA
BM-28442 NIGMS

SO JOURNAL OF CELL SCIENCE, 1997 Nov; 110 (Pt 22) 2875-84.
Journal code: 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; JOURNAL ARTICLE
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980206
Last Updated on STN: 20000303
Entered Medline: 19980127
AB The **alpha7beta1 integrin** is the primary laminin receptor on skeletal myoblasts and adult myofibers. It has distinct functions during muscle development and contributes to muscle structural integrity. We have studied this **integrin** in cases where expression of dystrophin or laminin are compromised. Immunofluorescence demonstrates an increase in **alpha7beta1** in patients with Duchenne **muscular dystrophy** and in mdx mice that lack dystrophin. Analysis of RNA from mdx mice and from patients with Duchenne and Becker **muscular dystrophies** indicates that the increase in the **alpha7beta1 integrin** is regulated at the level of **alpha7** gene **transcription**. In contrast, the levels of **alpha7beta1 integrin** are severely diminished in patients with laminin alpha2 chain congenital dystrophy **muscular dystrophy** and in dy/dy mice that also do not make the alpha2 laminin chain. Analysis of RNA from the hindlimbs of dy/dy mice demonstrated that in the absence of laminin **alpha7** gene **transcription** is inhibited and limited to specific alternatively spliced isoforms. We suggest that the increased expression of **alpha7beta1 integrin** in the absence of dystrophin compensates for the reduced dystrophin-mediated linkage of fibers with the basal lamina and modulates the development of pathology associated with these diseases. The decrease in **alpha7beta1 integrin** and its **transcripts** in the absence of laminin likely contributes to the severe myopathy that results from laminin alpha2 chain deficiency and suggests that laminin-2 regulates expression of the **alpha7 integrin** gene. The role of the **alpha7beta1 integrin** in muscle integrity also suggests that compromised expression of this receptor may underlie as yet undefined myopathies.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Fluorescent Antibody Technique, Indirect
Immunoblotting
***Integrins: BI, biosynthesis**
Mice
***Muscular Dystrophies: ME, metabolism**
***Muscular Dystrophy, Animal: ME, metabolism**
Polymerase Chain Reaction
CN 0 (**Integrins**); 0 (**integrin alpha7beta1**)

L23 ANSWER 33 OF 48 MEDLINE
AN **1998065331** MEDLINE
DN **98065331** PubMed ID: **9401799**
TI Light-microscopic study of the **beta 1 integrin** subunit in human skeletal muscle.
AU Heub S; Neundorfer B
CS Department of Neurology, Friedrich Alexander University of Erlangen-Nurnberg, Germany.
SO CLINICAL NEUROPATHOLOGY, 1997 Nov-Dec; 16 (6): 319-27.
Journal code: 8214421. ISSN: 0722-5091.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; JOURNAL ARTICLE
LA English

PS Priority Journals
EM 199811
ED Entered STN: 19981216
Last Updated on STN: 20000303
Entered Medline: 19980129

AB The **beta 1 integrin** subunit is identical with the CD29 antigen, which is found at the surface of leukocytes. **Integrins** are involved in cell-cell and cell-matrix adhesion, mediate neuronal attachment and neurite outgrowth in response to extracellular matrix proteins in cell culture systems. A few analyses of **beta 1 integrin** subunit have been done on developing and regenerating skeletal muscle in animals; but cell culture systems and animal models differ in some respects from human skeletal muscle in situ. The expression of a **beta 1 integrin** subunit variant in human skeletal muscle was reported merely by Western blot analysis. Our present study, performed with immunohistochemical procedures, attempts to demonstrate the expression of the **beta 1 integrin** subunit in developing, normal adult, and diseased human skeletal muscles. The results demonstrated that the **beta 1 integrin** subunit is expressed in developing, normal adult, regenerating, and denervated human skeletal muscle. In developing muscle, the **beta 1 integrin** subunit was observed in muscle cells at least from 12 to 16 weeks of gestation. In **muscular dystrophy** and inflammatory myopathy the **beta 1 integrin** subunit staining occurs in basophilic muscle fibers. Furthermore, the **beta 1 integrin** subunit is expressed in mature fast twitch type 2 fibers, and in denervated myocytes in neurogenic muscular atrophy. On serial sections, the **beta 1 integrin** subunit, N-CAM (neural cell adhesion molecule) and vimentin are expressed in identical muscle fibers. However, in mature fast twitch type 2 fibers the **beta 1 integrin** subunit is expressed exclusively and in neurogenic muscular atrophy vimentin expression is weak. In conclusion, the **beta 1 integrin** subunit, in human skeletal muscles, probably plays a role in the growth morphology and innervation of developing, regenerating, and denervated myocytes. Furthermore, the observation that the **beta 1 integrin** subunit is enriched in mature fast twitch type 2 fibers indicates that the **beta 1 integrin** subunits may play a role in transducing mechanical forces to extracellular matrix proteins.

CT Check Tags: Female; Human; Male
Adolescent
Adult
Aged
Aged, 80 and over
*Antigens, CD29: AN, analysis
Biological Markers
Biopsy
Child
Embryo and Fetal Development: PH, physiology
Gestational Age
*Microscopy: MT, methods
Middle Age
*Muscle, Skeletal: CH, chemistry
Muscle, Skeletal: EM, embryology
Muscle, Skeletal: PA, pathology
Muscular Atrophy: ME, metabolism
Muscular Atrophy: PA, pathology
Muscular Diseases: ME, metabolism
Muscular Diseases: PA, pathology
Muscular Dystrophies: ME, metabolism
Muscular Dystrophies: PA, pathology

Neural Cell Adhesion Molecules: AN, analysis
Regeneration: PH, physiology
*Vimentin: AN, analysis
CN 1 (Antigens, CD29); 2 (Biological Markers); 3 (Neural Cell Adhesion Molecules); 4 (Vimentin)

L83 ANSWER 34 OF 45 MEDLINE
AN 1998016417 MEDLINE
DN 98016417 PubMed ID: 9354797
TI Absence of **integrin alpha 7** causes a novel form of **muscular dystrophy**.
AU Mayer U; Saher G; Fassler R; Bornemann A; Echtermeyer F; von der Mark H; Miosge N; Poschl E; von der Mark K
CS Max-Planck-Institute for Biochemistry, Martinsried, Germany..
Mayer@biochem.mpg.de
SO NATURE GENETICS, (1997 Nov) 17 (3) 318-23.
Journal code: 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L25423
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19990129
Entered Medline: 19971204
AB **Integrin alpha 7 beta 1** is a specific cellular receptor for the basement membrane protein laminin-1 (refs 1,2), as well as for the laminin isoforms -2 and -4 (ref. 3). The **alpha 7** subunit is expressed mainly in skeletal and cardiac muscle and has been suggested to be involved in differentiation and migration processes during myogenesis. Three cytoplasmic and two extracellular splice variants that have been described are developmentally regulated and expressed in different sites in the muscle. In adult muscle, the **alpha 7A** and **alpha 7B** subunits are concentrated in myotendinous junctions but can also be detected in neuromuscular junctions and along the sarcolemmal membrane. To study the potential involvement of **alpha 7 integrin**, during myogenesis and its role in muscle integrity and function, we generated a null allele of the **alpha 7** gene (Itga7) in the germline of mice by homologous recombination in embryonic stem (ES) cells. Surprisingly, mice homozygous for the mutation are viable and fertile, indicating that the **alpha 7 beta 1 integrin** is not essential for myogenesis. However, histological analysis of skeletal muscle revealed typical symptoms of a progressive **muscular dystrophy** starting soon after birth, but with a distinct variability in different muscle types. The observed histopathological changes strongly indicate an impairment of function of the myotendinous junctions. These findings demonstrate that **alpha 7 beta 1 integrin** represents an indispensable linkage between the muscle fibre and the extracellular matrix that is independent of the dystrophin-dystroglycan complex-mediated interaction of the cytoskeleton with the muscle basement membrane.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
*Antigens, CD: GE, genetics
Antigens, CD: ME, metabolism
Extremities: PA, pathology
Flow Cytometry: MT, methods
Homozygote
Mice
Mice, Inbred Strains
Mice, Inbred mdx

Mice, Transgenic
Molecular Sequence Data
Muscle Fibers: PA, pathology
Muscle, Skeletal: PA, pathology
*Muscular Dystrophy, Animal: GE, genetics
Phagocytosis
Recombination, Genetic
Tenascin: ME, metabolism
Tendons: PA, pathology
CN 0 (Antigens, CD); 0 (ITGA7 protein, human); 0 (Tenascin)

L83 ANSWER 35 OF 45 MEDLINE
AN 1998012902 MEDLINE
DN 98012902 PubMed ID: 9352853
TI Relation between **integrin alpha7Bbeta1** expression in human intestinal cells and enterocytic differentiation.
AU Basora N; Vachon P H; Herring-Gillam F E; Perreault N; Beaulieu J F
CS Departement d'anatomie et de biologie cellulaire, Faculte de medecine, Universite de Sherbrooke, Quebec, Canada.
SO GASTROENTEROLOGY, (1997 Nov) 113 (5) 1510-21.
Journal code: 0374630. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
OS GENBANK-AF034833
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 20010303
Entered Medline: 19971113
AB BACKGROUND & AIMS: Cell-laminin interactions are principally mediated by specific membrane receptors of the **integrin** family. The **integrin alpha7beta1** is one of them. Its expression in the intestine has not yet been investigated although it appears to be a key element in muscle cell differentiation. In this study, the expression of its three known isoforms has been analyzed in developing and adult small intestine and in intestinal cell lines. METHODS: The expression of the **integrin alpha7beta1** was analyzed by indirect immunofluorescence, Western blotting, immunoprecipitation, and reverse-**transcription** polymerase chain reaction. RESULTS: The **alpha7B** isoform, but not the **alpha7A** and C isoforms, was detected in intestinal epithelial cells. In vivo, the presence of the **alpha7B** subunit was closely paralleled with (1) acquisition of differentiation characteristics during development and along the crypt-villus axis in the adult small intestine and (2) loss of enterocytic functions in the re-differentiated colonic epithelium. In vitro, the expression of **alpha7B** was also shown to correlate with the acquisition of enterocytic functions. In Caco-2 cells, the **alpha7Bbeta1 integrin** was found transiently up-regulated at the onset of sucrase-isomaltase expression. CONCLUSIONS: Taken together, these results suggest that **alpha7Bbeta1** expression is correlated with human intestinal cell differentiation.
CT Check Tags: Human; Support, Non-U.S. Gov't
Amino Acid Sequence
*Antigens, CD: AN, analysis
*Antigens, CD29: AN, analysis
Caco-2 Cells
Cell Differentiation
*Intestines: CH, chemistry
Intestines: CY, cytology
Molecular Sequence Data
*Receptors, Laminin: AN, analysis
Up-Regulation

CN + Antigens, CD ; + Antigens, CD29 ; + ITGA7 protein, human ; + Receptors, Laminin

L66 ANSWER 36 OF 45 MEDLINE
AN 97460018 MEDLINE
DN 97460018 PubMed ID: 9312189
TI **Integrins** (**alpha7beta1**) in muscle function and survival. Disrupted expression in merosin-deficient congenital **muscular dystrophy**.
AU Vachon P H; Xu H; Liu L; Loechel F; Hayashi Y; Arahata K; Reed J C; Wewer U M; Engvall E
CS The Burnham Institute, La Jolla Cancer Research Center, La Jolla, California 92037, USA.
SO JOURNAL OF CLINICAL INVESTIGATION, (1997 Oct 1) 100 (7) 1870-81. Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199710
ED Entered STN: 19971224
Last Updated on STN: 20000303
Entered Medline: 19971029
AB Mutations in genes coding for dystrophin, for alpha, beta, gamma, and delta-sarcoglycans, or for the alpha2 chain of the basement membrane component merosin (laminin-2/4) cause various forms of **muscular dystrophy**. Analyses of **integrins** showed an abnormal expression and localization of **alpha7beta1** isoforms in myofibers of merosin-deficient human patients and mice, but not in dystrophin-deficient or sarcoglycan-deficient humans and animals. It was shown previously that skeletal muscle fibers require merosin for survival and function (Vachon, P.H., F. Loechel, H. Xu, U.M. Wewer, and E. Engvall. 1996. J. Cell Biol. 134:1483-1497). Correction of merosin deficiency in vitro through cell transfection with the merosin alpha2 chain restored the normal localization of **alpha7beta1D integrins** as well as myotube survival. Overexpression of the apoptosis-suppressing molecule Bcl-2 also promoted the survival of merosin-deficient myotubes, but did not restore a normal expression of **alpha7beta1D integrins**. Blocking of **beta1 integrins** in normal myotubes induced apoptosis and severely reduced their survival. These findings (a) identify **alpha7beta1D integrins** as the de facto receptors for merosin in skeletal muscle; (b) indicate a merosin dependence for the accurate expression and membrane localization of **alpha7beta1D integrins** in myofibers; (c) provide a molecular basis for the critical role of merosin in myofiber survival; and (d) add new insights to the pathogenesis of neuromuscular disorders.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antigens, CD29: ME, metabolism
Cell Differentiation
Cell Survival
Cytoskeletal Proteins: BI, biosynthesis
Dystrophin: DF, deficiency
Dystrophin: GE, genetics
Hamsters
Immunohistochemistry
*Integrins: BI, biosynthesis
*Laminin: DF, deficiency
Laminin: GE, genetics
Membrane Glycoproteins: BI, biosynthesis
Mice
Mice, Inbred C57BL

Mice, Inbred mdx
Mice, Mutant Strains
*Muscle, Skeletal: PH, physiology
*Muscular Dystrophies: CN, congenital
Muscular Dystrophy, Animal: CN, congenital
Receptors, Laminin: BI, biosynthesis
Sarcolemma: ME, metabolism
Tissue Distribution
CN 0 (Antigens, CD29); 0 (Cytoskeletal Proteins); 0 (Dystrophin); 0 (Integrins); 0 (Laminin); 0 (Membrane Glycoproteins); 0 (Receptors, Laminin); 0 integrin alpha7beta1)

L83 ANSWER 37 OF 45 MEDLINE
AN 97453229 MEDLINE
DN 97453229 PubMed ID: 9307969
TI The laminin-binding activity of the **alpha 7** **integrin** receptor is defined by developmentally regulated splicing in the extracellular domain.
AU Ziober B L; Chen Y; Kramer R H
CS Department of Stomatology, University of California, San Francisco 94143-0512, USA.
NC DE-10306 (NIDCR
SO MOLECULAR BIOLOGY OF THE CELL, (1997 Sep) 8 (9) 1723-34.
Journal code: 9201390. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19980109
Last Updated on STN: 20000303
Entered Medline: 19971204
AB The expression pattern of the laminin-binding **alpha 7** **beta 1** **integrin** is developmentally regulated in skeletal, cardiac, and smooth muscle. The X1/X2 alternative splicing in the extracellular domain of **alpha 7** is found in the variable region between conserved alpha-chain homology repeat domains III and IV, a site implicated in ligand binding. To assess differences in X1/X2 isoform activity, we generated MCF-7 cell lines transfected with **alpha 7**-X1/X2 cDNAs. Transfectants expressing the **alpha 7**-X2 variant adhered rapidly to laminin 1, whereas those expressing **alpha 7**-X1 failed to attach. That **alpha 7**-X1 exists in an inactive state was established in assays using an activating **beta 1** antibody that induced X1-dependent cell adhesion and spreading. Furthermore, the activation of **alpha 7**-X1 was cell type specific, and when expressed in HT1080 cells, the **integrin** was converted into a fully functional receptor capable of promoting adhesion. Thus, the expression of the **alpha 7**-X1/X2 **integrin** is a novel mechanism that regulates receptor affinity states in a cell-specific context and may modulate **integrin**-dependent events during muscle development and repair.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
*Alternative Splicing
Breast Neoplasms
Carcinoma
Cell Adhesion: DE, drug effects
Cell Culture
Gene Expression Regulation, Developmental
Integrins: IM, immunology
*Integrins: ME, metabolism
Isomerism
*Laminin: ME, metabolism

Ligands
Manganese: PD, pharmacology
Protein Binding
*Receptors, Laminin: ME, metabolism
Tumor Cells, Cultured
RN 7439-96-5 (Manganese)
CN 0 (**Integrins**); 0 (Laminin); 0 (Ligands); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

L83 ANSWER 38 OF 45 MEDLINE
AN 97428300 MEDLINE
DN 97428300 PubMed ID: 9281377
TI The **alpha7beta1 integrin** mediates adhesion and migration of skeletal myoblasts on laminin.
AU Crawley S; Farrell E M; Wang W; Gu M; Huang H Y; Huynh V; Hodges B L; Cooper C N; Kaufman S J
CS Center for Neurobiology and Psychiatry, University of California at San Francisco, San Francisco, California 94143-0984, USA.
NC AG14683 (NIA)
AR41459 (NIAMS)
GM28842 (NIGMS)
SO EXPERIMENTAL CELL RESEARCH, (1997 Aug 25) 235 (1) 274-86.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19971013
Last Updated on STN: 19971013
Entered Medline: 19970930
AB Many aspects of myogenesis are believed to be regulated by myoblast interactions with specific components of the extracellular matrix. For example, laminin has been found to promote adhesion, migration, and proliferation of mammalian myoblasts. Based on affinity chromatography, the **alpha7beta1 integrin** has been presumed to be the major receptor mediating myoblast interactions with laminin. We have prepared a monoclonal antibody, G26, that specifically reacts with both the X1 and the X2 extracellular splice variants of the **alpha7 integrin** chain. This antibody completely and selectively blocks adhesion and migration of rat L8E63 myoblasts on laminin-1, but not on fibronectin. In contrast, a polyclonal antibody to the fibronectin receptor, alpha5beta1 **integrin**, blocks myoblast adhesion on fibronectin, but not on laminin-1. The **alpha7beta1 integrin** also binds to a mixture of laminin-2 and laminin-4, the major laminin isoforms in developing and adult skeletal muscle, but G26 is a much less potent inhibitor of myoblast adhesion on the laminin-2/4 mixture than on laminin-1. Based on affinity chromatography, we suggest that this may be due to higher affinity binding of **alpha7X1** to laminin-2/4 than to laminin-1.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Alternative Splicing
Antibodies, Monoclonal: PD, pharmacology
Antibody Specificity
CHO Cells
Cell Adhesion
Cell Line
Cell Movement
Fibronectins: ME, metabolism
Hamsters
Immunoblotting
Integrins: BI, biosynthesis
Integrins: IM, immunology

***Integrins: PH, physiology**
Kinetics
*Laminin: ME, metabolism
Mice
Muscle, Skeletal: CY, cytology
*Muscle, Skeletal: PH, physiology
Rats
Receptors, Fibronectin: IM, immunology
Receptors, Fibronectin: PH, physiology
*Receptors, Laminin: PH, physiology
Recombinant Proteins: BI, biosynthesis
Transfection
Variation (Genetics)
CN 0 (Antibodies, Monoclonal); 0 (Fibronectins); 0 (**Integrins**); 0 (Laminin); 0 (Receptors, Fibronectin); 0 (Receptors, Laminin); 0 (Recombinant Proteins); 0 (**integrin alpha7beta1**)

L83 ANSWER 39 OF 43 MEDLINE
AN **97227490** MEDLINE
DN **97227490** PubMed ID: **9132144**
TI Peripheral nerve involvement in merosin-deficient congenital **muscular dystrophy** and dy mouse.
AU Matsumura K; Yamada H; Saito F; Sunada Y; Shimizu T
CS Department of Neurology and Neuroscience, Teikyo University School of Medicine, Tokyo, Japan.. k-matsu@med.teikyo-u.ac.jp
SO NEUROMUSCULAR DISORDERS, (1997 Jan) 7 (1) 7-12. Ref: 50
Journal code: 9111470. ISSN: 0960-8966.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970507
Last Updated on STN: 20000303
Entered Medline: 19970501
AB Merosin, also called laminin-2, is an isoform of laminin comprised of the alpha 2, **beta 1** and gamma 1 chains. Deficiency of merosin alpha 2 chain was recently identified as the primary cause of the classical form of congenital **muscular dystrophy** (CMD), an autosomal recessive neuromuscular disorder characterised by **muscular dystrophy** and brain white matter abnormalities. Interestingly, merosin-deficient CMD and its animal model dy mouse are also accompanied by dysmyelination of peripheral motor nerves. In peripheral nerve, merosin is expressed in the endoneurium surrounding the Schwann cell/myelin sheath, while the putative merosin receptors dystroglycan and alpha 6 beta 4 **integrin** are expressed in the outer membrane of Schwann cell/myelin sheath. Together with the well known fact that the deposition of laminin in the basement membrane is essential for Schwann cell myelination, these findings indicate that the interaction of merosin with dystroglycan and/or alpha 6 beta 4 **integrin** plays an important role in peripheral myelinogenesis and that the disturbance of this interaction leads to peripheral dysmyelination in merosin deficiency. The clinical significance of peripheral dysmyelination in merosin deficiency is also discussed.
CT Check Tags: Animal; Support, Non-U.S. Gov't
*Laminin: DF, deficiency
Mice
*Mice, Mutant Strains: PH, physiology
Muscular Dystrophies: CN, congenital
***Muscular Dystrophies: ME, metabolism**
***Muscular Dystrophies: PP, physiopathology**

Muscular Dystrophy, Animal: GE, genetics
***Muscular Dystrophy, Animal: PP, physiopathology**
*Peripheral Nerves: PP, physiopathology
CN 1 (Laminin)

L88 ANSWER 40 OF 45 MEDLINE
AN 96411781 MEDLINE
DN 96411781 PubMed ID: 8810334
TI **Alpha7 integrin** mediates cell adhesion and migration on specific laminin isoforms.
AU Yao C C; Ziober B L; Squillace R M; Kramer R H
CS Department of Stomatology, Schools of Dentistry and Medicine, University of California San Francisco, 94143-0512, USA.
NC R01 CA38824 (NCI)
R01 DE10306 (NIDCR)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 11) 271 (41) 25598-603.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961119
Last Updated on STN: 20000303
Entered Medline: 19961119
AB The laminin-binding **alpha7beta1 integrin** receptor is expressed at high levels by skeletal and cardiac muscles and by certain melanocytic cells. We have assessed the potential role of the **alpha7A/B integrin** isoforms in mediating cell adhesion and motility and determined the laminin isoform specificity of this **integrin**. When MCF-7 breast carcinoma cells, normally nonadherent to laminin 1, were stably transfected with cDNA for mouse **alpha7**, they adhered with high efficiency and migrated on laminin 1 substrates. Function-perturbing monoclonal antibodies generated to mouse **alpha7** subunit blocked both adhesion and migration of **alpha7** transfectants on laminin 1 substrates. Additional studies with MCF-7 transfectants revealed that **alpha7beta1** binds well to laminin 1 and to a mixture of laminin 2 and 4 but not to laminin 5. Importantly, **alpha7beta1** was capable of promoting motility on both laminin 1 and laminin 2/4 substrates. However, MCF-7 cells transfected with cDNA for either **alpha7A** or **alpha7B** showed no significant differences in cell adhesion or motility on laminin 1 substrates. Although the role for the alternatively spliced cytoplasmic variants of **alpha7** remains unknown, the results establish that **alpha7beta1** mediates cell adhesive activities on a restricted number of laminin isoforms.
CT Check Tags: Animal; Female; Human; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antibodies, Monoclonal: PD, pharmacology
Antigens, CD: BI, biosynthesis
Antigens, CD: CH, chemistry
*Antigens, CD: PH, physiology
Base Sequence
Breast Neoplasms
*Cell Adhesion
Cell Line
Cell Movement
DNA Primers
Integrins: PH, physiology
Kinetics
*Laminin
Mice
Molecular Sequence Data

Recombinant Proteins: CH, chemistry
Recombinant Proteins: ME, metabolism
Transfection
CN (Antibodies, Monoclonal); 0 (Antigens, CD); 0 (DNA Primers); 0 (ITGA7 protein, human); 0 (**Integrins**; 0 (Laminin); 0 (Recombinant Proteins); 0 (**integrin alpha7beta1**)

L83 ANSWER 41 OF 45 MEDLINE
AN 95178218 MEDLINE
DN 95178218 PubMed ID: 7532981
TI Recognition of cryptic sites in human and mouse laminins by rat osteoclasts is mediated by beta 3 and **beta 1 integrins**.
AU Horton M A; Spragg J H; Hodary S C; Helfrich M H
CS I.C.R.F. Haemopoiesis Group, St. Bartholomew's Hospital, London, UK.
SO BONE, (1994 Nov-Dec) 15 (6) 639-46.
Journal code: 8500748. ISSN: 8756-3282.
CY United States
DT Journal; Article; JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950419
Last Updated on STN: 19960129
Entered Medline: 19950403
AB Laminins may be encountered by osteoclasts and their precursors in basement membranes when they migrate from periosteal vasculature during skeletal development and in pathological situations. We have examined the recognition by osteoclasts of intact laminins and their proteolytic derivatives, and analysed the mechanism of adhesion. Rat osteoclasts fail to bind intact mouse Engelbreth-Holm-Swarm (EHS) laminin (3% adhesion relative to adhesion to foetal calf serum proteins) and bind only weakly to native human placental laminin (13%) or human merosin (9%). Pepsin treatment of native mouse EHS and human laminins increased osteoclast adhesion. Rat osteoclasts adhered to mouse EHS laminin-derived P1 fragment (70%), but failed to bind the E8 fragment, which contains adhesion sites recognised by some **integrins**. Binding to human and mouse P1 laminins was abolished by treatment with RGD-containing peptides and required divalent cations, but not by YIGSR peptide. Combinations of monoclonal antibodies to rat beta 3 and alpha v **integrins** reduced binding to P1 fragment by 91% and to human laminin by 72%, demonstrating that the major **integrin** involved in rat osteoclast adhesion to proteolysed laminin is alpha v beta 3. Antiserum to **beta 1 integrin** inhibited adhesion to human laminin by 40%, but to P1 fragment by only 8%; this suggests that **beta 1 integrins**(s) contribute to osteoclast adhesion to human laminin but probably not to P1 fragment. The involvement of alpha v beta 3 **integrin** was confirmed using a recombinant human alpha v beta 3 solid phase binding assay, alpha v beta 3 bound to mouse P1 fragment and proteolytically digested human laminin, but not intact laminins. (ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Antibodies, Monoclonal
Binding, Competitive
Cations, Divalent
Cell Adhesion: DE, drug effects
Integrins: IP, isolation & purification
***Integrins: ME, metabolism**
Laminin: CH, chemistry
*Laminin: ME, metabolism
Mice
Molecular Sequence Data

Oligopeptides: ME, metabolism
*Osteoclasts: ME, metabolism
Peptide Fragments: CH, chemistry
*Peptide Fragments: ME, metabolism
Platelet Glycoprotein GPIIb-IIIa Complex
Rats
Receptors, Cytoadhesin: IP, isolation & purification
Receptors, Cytoadhesin: ME, metabolism
*Receptors, Laminin: ME, metabolism
Receptors, Vitronectin
Recombinant Proteins: IP, isolation & purification
Recombinant Proteins: ME, metabolism
Snake Venoms: ME, metabolism

RN 111590-64-2 (tyrosyl-isoleucyl-glycyl-seryl-arginine); 99896-85-2 (arginyl-glycyl-aspartic acid)

CN 0 (Antibodies, Monoclonal); 0 (Cations, Divalent); 0 (**Integrins**); 0 (Laminin); 1 (Oligopeptides); 0 (Peptide Fragments); 0 (Platelet Glycoprotein GPIIb-IIIa Complex); 0 (Receptors, Cytoadhesin); 0 (Receptors, Laminin); 0 (Receptors, Vitronectin); 0 (Recombinant Proteins); 0 (Snake Venoms); 0 (**integrin alpha7beta1**)

L83 ANSWER 42 OF 45 MEDLINE
AN 94230598 MEDLINE
DN 94230598 PubMed ID: 8175907
TI Selective modulation of the interaction of **alpha 7 beta 1 integrin** with fibronectin and laminin by L-14 lectin during skeletal muscle differentiation.
AU Gu M; Wang W; Song W K; Cooper D N; Kaufman S J
CS Department of Cell and Structural Biology, University of Illinois, Urbana 61801.
NC GM-28842 (NIGMS)
SO JOURNAL OF CELL SCIENCE, (1994 Jan) 107 (Pt 1) 175-81.
Journal code: 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940620
Last Updated on STN: 19970203
Entered Medline: 19940606

AB The **alpha 7 beta 1 integrin** was originally identified and isolated from differentiating skeletal muscle and shown to be a laminin-binding protein (Song et al. (1992) J. Cell Biol. 117, 643-657). Expression of the **alpha 7** gene and protein are developmentally regulated during skeletal muscle differentiation and have been used to identify cells at distinct stages of the myogenic lineage (George-Weinstein et al. (1993) Dev. Biol. 156, 209-229). The lactoside-binding protein L-14 exists as a dimer and has been localized on a variety of cells, in association with extracellular matrix. During myogenesis in vitro, L-14 is synthesized within replicating myoblasts but it is not secreted until these cells commence terminal differentiation and fusion into multinucleate fibers (Cooper and Barondes, J. Cell Biol. (1990) 110, 1681-1691). Addition of purified L-14 to myogenic cells plated on laminin inhibits myoblast spreading and fusion, suggesting that the L-14 lectin regulates muscle cell interactions with the extracellular matrix that are germane to myogenic development (Cooper et al. (1991) J. Cell Biol. 115, 1437-1448). We demonstrate here, using affinity chromatography and immunoblots, that **alpha 7 beta 1** also binds to fibronectin and to the L-14 lectin. L-14 binds to both laminin and to the **alpha 7 beta 1 integrin**, and it can effectively inhibit the association of

laminin and this **integrin**. Modulation of **alpha 7 beta 1** interaction with its ligands by L-14 is selective; L-14 does not bind to fibronectin, nor does it interfere with the binding of fibronectin to **alpha 7 beta 1**. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Cell Differentiation
Cell Line
Chromatography, Affinity
Electrophoresis, Polyacrylamide Gel
*Fibronectins: ME, metabolism
Galectin 1
Hemagglutinins: BI, biosynthesis
*Hemagglutinins: ME, metabolism
Immunoblotting
Integrins: IP, isolation & purification
***Integrins: ME, metabolism**
*Laminin: ME, metabolism
Molecular Weight
*Muscles: CY, cytology
Muscles: ME, metabolism
Protein Binding
Rats
Receptors, Laminin: ME, metabolism
Recombinant Proteins: IP, isolation & purification
Recombinant Proteins: ME, metabolism
Tumor Cells, Cultured

CN 0 (Fibronectins ; 0 (Galectin 1); 0 (Hemagglutinins); 0 (**Integrins**); 0 (Laminin); 0 (Receptors, Laminin); 0 (Recombinant Proteins); 0 (**integrin alpha7beta1**

L83 ANSWER 43 OF 45 MEDLINE
AN 94110297 MEDLINE
DN 94110297 PubMed ID: 8262763
TI **Alpha 7 beta 1 integrin** is a component of the myotendinous junction on skeletal muscle.
AU Bao Z Z; Lakonishok M; Kaufman S; Horwitz A F
CS Department of Biochemistry, University of Illinois at Urbana-Champaign IL 61801.
NC GM 23244 (NIGMS)
SO JOURNAL OF CELL SCIENCE, (1993 Oct) 106 (Pt 2) 579-89.
Journal code: 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199402
ED Entered STN: 19940228
Last Updated on STN: 19940228
Entered Medline: 19940214
AB Immunization against a 71 kDa band that co-purifies with skeletal muscle **integrins** has resulted in an antibody directed against the avain **alpha 7 integrin** subunit. The specificity of the antibody was established by patterns of tissue staining and cross-reactivity with antibodies directed against the cytoplasmic domain of the rat **alpha 7** cytoplasmic domain. In sections of adult skeletal muscle the **alpha 7 integrin** was enriched in the myotendinous junction (MTJ). This localization was unique as neither the alpha 1, alpha 3, alpha 5, alpha 6 and alpha v subunit localizes in the myotendinous junction. The distribution of the **alpha 7** subunit in the MTJ was examined during embryonic development. **alpha 7** expression in the junction is first apparent around embryo day 14 and is almost exclusively at the

developing MTJ at this stage. alpha 5 is expressed with distinctive punctate staining around the junctional area in earlier embryos (11-day). The time of appearance of the **alpha 7** subunit in the MTJ correlates with the insertion of myofibrils into subsarcolemmal densities and folding of the junctional membrane, suggesting a role of the **alpha 7 integrin** in this process. Vinculin is present throughout development of the myotendinous junction, suggesting that the **alpha 7 integrin** recognizes a preformed cytoskeletal structure. The presence of the **alpha 7** subunit in the myotendinous junction and the alpha 5 subunit in the adhesion plaque demonstrates a molecular difference between these two adherens junctions. It also points to possible origins of junctional specificity on muscle. Differences between these two junctions were developed further using an antibody against phosphotyrosine (PY20). Phosphotyrosine is thought to participate in the organization and stabilization of adhesions. The focal adhesion and the neuromuscular junction, but not the MTJ, contained proteins phosphorylated on tyrosine.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antibodies, Monoclonal
Chick Embryo
Chickens
Fluorescent Antibody Technique
Integrins: GE, genetics
Integrins: IM, immunology
***Integrins: ME, metabolism**
Mice
Molecular Sequence Data
Muscles: EM, embryology
*Muscles: ME, metabolism
Rats
Tendons: EM, embryology
*Tendons: ME, metabolism
Tissue Distribution

CN 0 (Antibodies, Monoclonal); 0 (**Integrins**); 0 (**integrin alpha7beta1**)

L83 ANSWER 44 OF 45 MEDLINE
AN 93366324 MEDLINE
DN 93366324 PubMed ID: 8360188
TI A new isoform of the laminin receptor **integrin alpha 7 beta 1** is developmentally regulated in skeletal muscle.
AU Collo G; Starr L; Quaranta V
CS Department of Cell Biology, Scripps Research Institute, La Jolla, California 92037.
NC CA47858 (NCI)
GM46902 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Sep 5) 268 (25) 19019-24.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L16844
EM 199309
ED Entered STN: 19931015
Last Updated on STN: 19970203
Entered Medline: 19930927
AB Within the **integrin** family, there are two groups of receptors that bind laminin. One of these groups comprises the heterodimers alpha 6 **beta 1**, alpha 6 **beta 1**, and **alpha 7 beta 1**, all of which bind

the E8 fragment of laminin, and whose alpha subunits show significant homology at the amino acid sequence level. alpha 3 and alpha 6 exist as isoforms with distinct cytoplasmic domains (termed A and B), suggesting that they may couple laminin adhesion to distinct cellular responses. We report the identification of a new **alpha 7** mRNA which encodes an **alpha 7** protein isoform with an alternative cytoplasmic domain. Based on homology with alpha 3 and alpha 6 isoforms, this new isoform is classified as **alpha 7A** and the previously published one as **alpha 7B**. This result extends the similarity between alpha 3, alpha 6, and **alpha 7** laminin receptor subunits and suggests a common ancestral gene. The **alpha 7 beta 1** laminin receptor was proposed to be involved in myogenic differentiation. However, **alpha 7** isoforms were not investigated in that context. We detected the **alpha 7B** isoform mRNA in all tissues and cell types tested, including myocardial and skeletal muscle. In contrast, the **alpha 7A** isoform was detectable exclusively in skeletal muscle, not in myocardial muscle or cells or any other tissues or cell lines tested. Furthermore, the differentiating skeletal muscle cell line C2C12 expressed only **alpha 7B** at the replicating myoblast stage and acquired **alpha 7A** expression upon induction of differentiation and fusion. Splicing of **alpha 7B** mRNA in C2C12 occurred shortly after myogenin expression and could be an indicator of progression through the program of skeletal muscle differentiation.

CT Check Tags: Animal; Female; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
Cell Differentiation
***Gene Expression Regulation**
Integrins: CH, chemistry
***Integrins: GE, genetics**
Integrins: ME, metabolism
Kinetics
*Laminin: ME, metabolism
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
Molecular Sequence Data
*Muscle Development
Muscles: CH, chemistry
Muscles: ME, metabolism
Myocardium: CH, chemistry
Myocardium: ME, metabolism
Organ Specificity
Polymerase Chain Reaction
RNA Splicing
RNA, Messenger: AN, analysis
RNA, Messenger: ME, metabolism

CN 0 (**Integrins**); 0 (Laminin); 0 (RNA, Messenger); 0 (**integrin alpha7beta1**)

L46 ANSWER 46 OF 46 MEDLINE
AN **93139147** MEDLINE
DN **93139147** PubMed ID: **1283164**
TI Co-localization and molecular association of dystrophin with laminin at the surface of mouse and human myotubes.
AU Dickson G; Abad A; Morris G E; Simon H; Noursadeghi M; Walsh F S
CS Department of Experimental Pathology, UMDS, Guy's Hospital, London Bridge, UK.
SO JOURNAL OF CELL SCIENCE, 1992 Dec 113 (Pt 4) 1223-33.
Journal code: 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom

DT Journal; Article; JOURNAL ARTICLE
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990312
Last Updated on STN: 19960129
Entered Medline: 19990224

AB In Duchenne **muscular dystrophy** (DMD), deficiency of the protein dystrophin results in necrosis of muscle myofibres, associated with lesions in the sarcolemma and surrounding basal lamina. Dystrophin has been proposed to be a major component of the sub-sarcolemmal cytoskeleton involved in maintaining the integrity of the myofibre plasma membrane, and is known to associate with a group of sarcolemmal glycoproteins, one of which exhibits high affinity binding to the basal lamina component laminin. However, a direct or indirect transmembrane association of dystrophin in muscle cells with the myofibre basal lamina has not been demonstrated. To address this question we have examined dystrophin immunostaining and immunoprecipitation patterns in cultured mouse and human myotubes in comparison with that of the basal lamina component, laminin. Dual-immunolabelling revealed virtually complete co-localization of dystrophin on the inside surface of the muscle cell sarcolemma with plaques and veined arrays of laminin accumulating on the extracellular face. This pattern of laminin and dystrophin distribution was distinct from that of other cell surface molecules expressed in myotubes such as the neural cell adhesion molecule, NCAM, and the **beta 1 integrin** receptor, and immunoprecipitation of dystrophin from solubilized myotube extracts resulted in co-purification of laminin B1 chain confirming an association between these two components. The results thus provide the first direct cellular evidence of a transmembrane linkage between dystrophin in the sarcolemmal cytiskeleton with laminin in the overlying basal lamina. While the immunocytochemical distribution of laminin was apparently normal in dystrophin-deficient muscle cells, elevated levels of soluble laminin were present in extracts of mdx compared with normal mouse skeletal muscle. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Antigens, CD29
Cell Adhesion Molecules, Neuronal: AN, analysis
Cells, Cultured
*Dystrophin: AN, analysis
Dystrophin: IP, isolation & purification
Integrins: AN, analysis
*Laminin: AN, analysis
Laminin: IP, isolation & purification
Mice
Mice, Inbred C57BL: ME, metabolism
Mice, Mutant Strains
Microscopy, Fluorescence
Molecular Sequence Data
*Muscle Proteins: AN, analysis
*Muscles: CH, chemistry
Muscular Dystrophy, Animal: ME, metabolism
Peptide Fragments: IM, immunology
*Sarcolemma: CH, chemistry

CN [illegible] Antigens, CD29.; [illegible] Cell Adhesion Molecules, Neuronal.; [illegible] Dystrophin.; [illegible] **Integrins**.; [illegible] Laminin.; [illegible] Muscle Proteins.; [illegible] Peptide Fragments.

=> fil wpix
FILE 'WPIX' ENTERED AT 12:19:14 ON 19 MAY 2010

FILE LAST UPDATED: 5 MAY 2003 <20030505/UP>
MOST RECENT DERWENT UPDATE: 200329 <200329/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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=> d all abeq tech abex 198

L98 ANSWER 1 OF 1 WPIX (C) 2003 THOMSON DERWENT
AN **2002-674967** [72] WPIX
DNN **N2002-533677** DNC **C2002-190172**
TI Identifying individual exhibiting symptoms of **muscular dystrophy**, for diagnosing and treating **muscular dystrophy**, by detecting transcription or translation product of **alpha7beta1 integrin** gene in a tissue sample.
DC B04 D16 S03
IN KAUFMAN, S J
PA (KAUF-I) KAUFMAN S J; (UNII) UNIV ILLINOIS FOUND
CYC 99
PI WO 2002066989 A2 20020829 (200272)* EN 53p G01N033-68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002192710 A1 20021219 (200303) G01N033-53
ADT WO 2002066989 A2 WO 2002-US6376 20020220; US 2002192710 A1 Provisional US 2001-270645P 20010220, Provisional US 2001-286890P 20010427, US 2002-81885 20020220
PRAI US 2001-286890P 20010427; US 2001-270645P 20010220; US 2002-81885 20020220
IC ICM G01N033-53; G01N033-68
ICS A61K048-00; **A61P021-00**; C12N005-00; C12N015-10; C12Q001-68
AB WO 2002066989 A UPAB: 20021108
NOVELTY - Identifying (M1) symptoms of **muscular dystrophy** (MD) in individual suffering from **scapuloperoneal muscular dystrophy** (SPMD), comprises detecting a transcription or translation product of an **alpha 7 beta 1 integrin** gene in a tissue sample.
DETAILED DESCRIPTION - Identifying (M1) symptoms of **muscular dystrophy** (MD) in individual suffering from **scapuloperoneal muscular dystrophy** (SPMD), comprises detecting a transcription or translation product of an

alpha 7 beta 1 integrin
gene in a tissue sample. (M1) comprises:
(a) obtaining a tissue sample from an individual exhibiting symptoms of a **dystrophy**, where the sample is obtained from a tissue known in a normal individual to express **alpha 7 beta 1 integrin**;
(b) detecting a transcription or translation product of an **alpha 7 beta 1 integrin** gene in the sample; and
(c) determining a level of the transcription or translation product of the **alpha 7 beta 1 integrin** gene in the sample as compared with a level in a tissue sample from the same tissue of a normal individual. SPMD is diagnosed when the tissue sample of the individual exhibiting MD symptoms, comprises a level of a transcription or translation product of the **alpha 7 beta 1 integrin** gene in the tissue sample that is lower than the level in a tissue sample from the same tissue of a normal individual.
INDEPENDENT CLAIMS are also included for:
(1) a reporter gene construct (I) comprising a transcription regulatory sequence of a human alpha 7 **integrin** gene and a reporter coding sequence;
2) a recombinant host cell (II) comprising the reporter gene construct;
3) identifying (M2) a composition that increases expression of an alpha 7 **integrin** gene, comprises:
a) contacting the recombinant host cell with a test composition to produce a contacted recombinant host cell;
b) monitoring reporter coding expression in the contacted recombinant host cell and monitoring expression of the reporter coding sequence of the reporter gene construct in a recombinant host cell that has not been contacted with the test composition; and
c) determining if the test composition increases reporter coding sequence expression when the expression of the reporter coding sequence is greater in the contacted host cell than in the recombinant host cell that has not been contacted with the test composition, where a composition that increases the expression of an alpha 7 **integrin** gene is identified when the expression of the reporter coding sequence is greater in the contacted host cell than in the recombinant host cell that has not been contacted with the test composition;
(4) alleviating (M4) symptoms of MD having:
(a) alpha 7 **integrin** levels that are lower in a patient suffering from or susceptible to MD than in a normal individual, comprises administering to the patient the composition identified by(M3); or
(b) levels of alpha 7 **integrin**, **dystrophin** and.or utrophin that are lower in a patient suffering from or susceptible to MD than in a normal individual, comprises administering to the patient a DNA construct comprising an alpha 7 **integrin** coding sequence operably linked to a transcription regulatory sequence that enables selective expression in muscle cells and a vector sequence.
ACTIVITY - Inotropic.
No biological data given.
MECHANISM OF ACTION - Gene therapy.
USE - (M1-4) are useful for diagnosing, ameliorating and treating **muscular dystrophy** symptoms such as **scapuloperoneal muscular dystrophy** or Duchenne **muscular dystrophy**. The nucleic acid probes, primers or immunological probes can be used for detecting the reduction of or lack of expression of the **alpha 7 beta 1 integrin** in SPMD.
Dwg.0/12
FS CPI EPI
FA AB; DCN

MD OPI: B04-E05; B04-E06; B04-E12; B04-F1200E; B04-F07T1E; B11-C07A;
B11-C08E3; B11-C08E5; B11-C08F2; B12-K04A; B12-K14E; B11-K14F;
B14-C05E; B14-S03; D08-H04; D08-H12D1; D08-H12E; D15-H14B4
EPI: S03-E14H1; S03-E14H4; S03-E14H6
TECH UPTX: 20021108
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The translation product of an **alpha7beta1 integrin** gene in the tissue sample is detected by contacting the tissue sample using an **alpha7beta1 integrin**-specific antibody that is detectably labeled. A transcription product of an **alpha7beta1 integrin** gene is detected in the tissue sample using reverse transcriptase-polymerase chain reaction (RT-PCR). The primers used in the RT-PCR comprise a sequence of (S4) and (S5). In (M2), where the monitoring and determining steps are carried out in high throughput assay format. In the method of (4), where the MD is Duchenne **muscular dystrophy**. The vector sequence is a virus vector sequence or a plasmid sequence. Administering comprises ex vivo transformation of stem cells or myoblasts isolated from the patient to produce transformed myoblasts and subsequent administration of the transformed stem cell or transformed myoblasts to the patient with the result that the transformed myoblasts differentiate to form muscle cells that express alpha7 **integrin**, where the symptoms of MD is ameliorated.
Preferred Gene Construct: The reporter coding sequence is selected from the group of a green fluorescent protein, luciferase, beta-lactamase, beta-galactosidase, or beta-glucuronidase, or an immunological tag portion. The transcription regulatory sequence comprises a sequence of 1870 base pairs fully defined in the specification. The reporter gene construct further comprises a vector sequence.
Preferred Host Cell: The cell is preferably a cultured muscle cell.
GAACAGCAGTTTCTGGAGG (S4)
CCTTGAACTGCTGTCGGTCT (S5)
ABEX UPTX: 20021108
ADMINISTRATION - Administration may be intravenous, intramuscular or by regional perfusion (all claimed). No dosage details given.

EXAMPLE - No suitable example given.

=> d his

(FILE 'HOME' ENTERED AT 11:24:23 ON 13 MAY 2003)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:24:37 ON 13 MAY 2003
E INTEGRIN/CT
L1 55 S INTEGRIN (L) (ALPHA7 OR ALPHAVII OR ALPHA(W)7 OR VII))(W)'BETA
E MUSCULAR DYSTROPHY/CT
L2 4381 S E3-E18
E E3+ALL
L3 6000 S E6,E5
L4 7113 S E5,E7/BI
L5 7617 S MUSCUL? DYSTROPH?
L6 11 S SCAPULOPERONEAL?
L7 13 S L1 AND L2-L6
L8 7 S INTEGRIN(L)'ALPHA7BETA1' OR ALPHA7BETA1 OR ALPHAVIIBETA1 OR AL
L9 1 S L8 AND L2-L6
L10 13 S L7,L9
L11 146 S INTEGRIN? L ALPHA 7#
L12 32 S INTEGRIN? L ALPHA7?
L13 7168 S INTEGRIN? L BETA 1
L14 480 S INTEGRIN? L BETA1
L15 34 S L2-L6 AND L11-L14
L16 18 S L15 AND L11,L12 AND L13,L14

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L17            16 S L10,L16
                  E KAUFMAN S/AU
L18           113 S E3,E10
                  E KAUFMAN STEPHEN/AU
L19            53 S E3,E7,E8
L20             1 S E2
L21             5 S L17 AND L18-L20
                  E DIAGNOSIS/CT
                  E L17 AND E3+NT
                  E DIAGNOSIS/CT
L22             2 S L17 AND E3+NT
L23             2 S L17 AND E3-E18
                  E E3+ALL
L24             2 S L17 AND E10+NT

     FILE 'HCAPLUS' ENTERED AT 11:36:03 ON 13 MAY 2003
                  E ANIMAL TISSUE/CT
                  E E3+ALL
L25            15 S L17 AND E3,E4,E2+NT
                  E ANIMAL TISSUE/CT
                  E E22+ALL
L26             1 S L17 AND E2,E3,E1+NT
L27             2 S L25,L26 AND L22-L24
L28            18 S L17,L21-L24,L25-L27
                  SEL [illegible] AN 1 8 9
L29            15 S L28 NOT E1-E7
L30            15 S L29 AND L1-L29
L31            15 S L30 AND INTEGRIN?
L32            15 S L31 AND DYSTROPH?
L33             2 S L32 AND (DIAGNOS? OR PROGNOS? OR PREDICT?)
L34             3 S L32 AND SCREEN?
L35             3 S L33,L34
L36            12 S L32 NOT L35

     FILE 'HCAPLUS' ENTERED AT 11:43:18 ON 13 MAY 2003

     FILE 'BIOSIS' ENTERED AT 11:44:04 ON 13 MAY 2003
                  E KAUFMAN S/AU
L37           487 S E3,E12
L38            34 S E43,E46,E51
L39         11247 S L4 OR L5 OR L6
L40            68 S L1 OR L8
L41            13 S L39 AND L40
L42             8 S L37,L38 AND L39
L43            16 S L37,L38 AND L40
L44             4 S L41 AND L42,L43
L45            13 S L41,L44
L46            13 S L42,L43 NOT L45
L47            13 S L45 AND INTEGRIN
L48            13 S L47 AND (ALPHA7? OR ALPHA 7# OR BETA1 OR BETA 1)
L49            13 S L46 AND INTEGRIN
L50            13 S L49 AND (ALPHA7? OR ALPHA 7# OR BETA1 OR BETA 1)
L51            26 S L41-L50

     FILE 'HCAPLUS, BIOSIS' ENTERED AT 11:48:55 ON 13 MAY 2003
L52            29 DUP REM L36 L51 (9 DUPLICATES REMOVED)

     FILE 'HCAPLUS, BIOSIS' ENTERED AT 11:49:42 ON 13 MAY 2003

     FILE 'MEDLINE' ENTERED AT 11:50:13 ON 13 MAY 2003
L53         15124 S L4-L11
                  E MUSCULAR DYSTROPHY/CT
                  E E3+ALL
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                     E E2+ALL
L54          15166 S E15+NT
                     E MUSCULAR DYSTROPHY CT
                     E E4+ALL
L55           2429 S E3+NT
L56          17663 S L53-L55
L57             54 S L1 OR L8
L58           5149 S INTEGRIN AND (ALPHA7? OR ALPHA 7# OR BETA1 OR BETA 1[illegible]
L59             37 S L56 AND L57
L60             53 S L56 AND L58
L61             53 S L59,L60
L62              1 S L61 AND DI/CT
L63             14 S L61 AND E1./CT
                     E PROGNOSIS/CT
                     E E[illegible]+ALL
L64              0 S L61 AND E3+NT
L65             14 S L62,L63
L66              2 S L61 AND SCREEN?
L67             15 S L65,L66
L68              8 S L61 AND ANTIBODIES+NT/CT
L69              4 S L67 AND L68
L70             11 S L67-L69
L71             [illegible] S L61 AND (TRANSCRIPT? OR TRANSLAT?)
L72             16 S L70,L71
L73             16 S L62-L72
L74             37 S L61 NOT L73
L75             16 S L61 AND G5./CT
L76             15 S L75 AND L73
L77             11 S L71 AND L74
L78             26 S L76,L77
L79             37 S L57 AND L62-L78
L80             16 S L59-L78 NOT L79
                     SEL DN AN 1 5 10 11 13 14 15 16
L81              8 S L80 AND E1-E24
L82              5 S L78,L81 AND BIOPS?
L83             45 S L79,L81,L82

     FILE 'MEDLINE' ENTERED AT 12:03:45 ON 13 MAY 2003

     FILE 'WPIX' ENTERED AT 12:03:56 ON 13 MAY 2003
L84              6 S L1/BIX OR L8/BIX
L85             19 S (B04-H21 OR C04-H21)/MC
L86             27 S L84,L85
L87              0 S L86 AND (ALPHA7BETA1 OR ((ALPHA7# OR ALPHA 7#) AND (BETA1 OR[illegible]
L88           1255 S L4/BIX OR L5/BIX OR L6/BIX
L89           1095 S INTEGRIN/BIX
L90              5 S L86,L89 AND L88
L91            127 S A61P021/IC,ICM,ICS,ICA,ICI AND L86,L88
L92            126 S L91 AND ?DYSTROPH?/BIX
L93           1096 S L84-L86,L89
L94              5 S L88 AND L93
L95             11 S A61P021/IC,ICM,ICS,ICA,ICI AND L93
L96             26 S ?DYSTROPH?/BIX AND L93
L97             34 S L94-L96
                     SEL DN AN 5
L98              1 S L97 AND E25-E27
L99              7 S L84 NOT L98

     FILE 'WPIX' ENTERED AT 12:19:19 ON 13 MAY [illegible]

     FILE 'WPIX' ENTERED AT 12:19:16 ON 13 MAY [illegible]
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